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The JOURNAL of VENEREAL DISEASE INFORMATION

Volume 30 January 1949 Number 1

ORIGINAL ARTICLES

Results of Therapy by Race, Sex, and Stage of Syphilis 1
Theodore J. Bauer, *Medical Director*
Eleanor V. Price, *Biostatistician*

Asexual Syphilis in Children 7
Henry Eisenberg, *Surgeon (R)*
Frederick Plotke, M. D., M. P. H.
Amelia H. Baker, M. A.

Comparative Studies on Mailed Spinal Fluid Specimens 11
George R. Cannefax, *Bacteriologist*
George E. Parkhurst, *Senior Surgeon*
Richard W. Bowman, *Biostatistician*

Integration of Public Health Nursing Into a Marine Hospital . . . 15
J. A. Trautman, *Senior Surgeon*
Rosalie Giacomo, *Senior Assistant Nurse Officer*

Problems of Out-Patient Management of Syphilis in the South . . . 19
John A. Lewis, Jr., *Surgeon*

CURRENT LITERATURE 22

CURRENT NOTES AND REPORTS 30

STATISTICS

Venereal Disease Cases Reported by Disease and Stage, Fiscal 1948 . 32

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Public Health Service

Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in the JOURNAL OF VENEREAL DISEASE INFORMATION, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the JOURNAL, and should be presented on separate sheets, rather than within text material.

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Chief, Division of Venereal Disease

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Results of Therapy by Race, Sex, and Stage of Syphilis

Theodore J. Bauer, Medical Director,[1] and Eleanor V. Price, Biostatistician, United States Public Health Service

Numerous studies have been conducted to evaluate results of therapy for early syphilis. Although fairly uniform results have been reported by some investigators, wide differences exist among others. One of the principal causes for the variation in results has been the lack of uniformity in the statistical methods used for analysis. This has been adequately covered by Iskrant et al. (*1*). It is the purpose of the present paper to determine what influence the factors of race, sex, and stage of syphilis might have exerted on the results reported.

From material submitted to the United States Public Health Service for evaluation, records from the two rapid treatment centers with the greatest volume of cases and the highest percentage of posttreatment observation have been selected for analysis. The study includes 6,310 patients treated prior to 1947, and is limited to previously untreated primary and secondary syphilis. The rate of posttreatment observation at the twelfth month is 75 percent (ranging from 73 to 78 percent in the race-sex groups and from 74 to 81 percent for the stages of syphilis).

One difficulty encountered in any evaluation is the uneven distribution of the race-sex groups in the various stages of syphilis. In the entire 6,310 cases, there are only 11 white females with the diagnosis of seronegative primary syphilis (table 1). Although the total cases are about evenly divided between males (54 percent) and females (46 percent), they are predominantly Negro (80 percent) and predominantly secondary syphilis (66 percent).

Table 1.—*Distribution of cases by race, sex, and stage of syphilis*

Race and sex	Stage of syphilis							
	Seronegative primary		Seropositive primary		Secondary		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
White male	126	2.0	265	4.2	397	6.3	788	12.5
White female	11	.2	62	1.0	378	6.0	451	7.1
Negro male	491	7.8	918	14.5	1,228	19.5	2,637	41.8
Negro female	71	1.1	224	3.5	2,139	33.9	2,434	38.6
Total	699	11.1	1,469	23.3	4,142	65.6	6,310	100.0

The over-all results of therapy, based on a total of all schedules of treatment and measured by cumulative percentage of cases re-treated (including reinfection, clinical relapse, and serorelapse or resistance) through 24 months of posttreatment observation, are presented in Charts 1 and 2.

Chart 1 is a comparison of results by stage of syphilis. In the white male group, the re-treatment rate for patients treated for secondary syphilis is more than double the rates for patients treated for either seronegative or seropositive primary syphilis from the eigbth month

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[1] Chief, Division of Venereal Disease.

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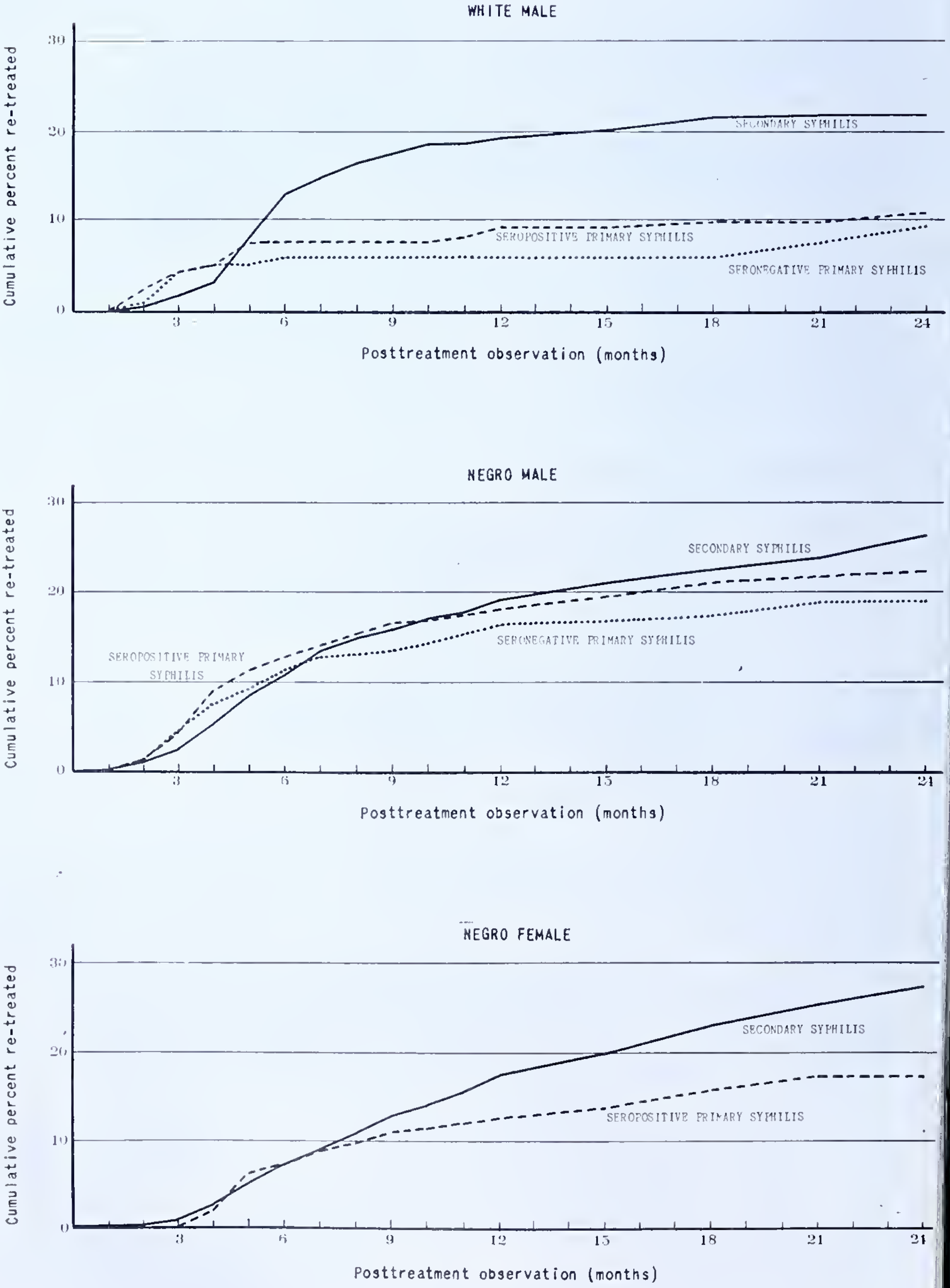
CHART I

INFLUENCE OF STAGE OF DISEASE ON RESULTS OF THERAPY FOR EARLY SYPHILIS

TOTAL OF ALL SCHEDULES OF THERAPY



through the remainder of the 24 months of observation.[2] The re-treatment rates for seronegative primary, seropositive primary, and secondary syphilis at the eighth month are 6.0, 7.6, and 16.1 percent, respectively; and at the twenty-fourth month, 9.2, 10.6, and 21.8 percent, respectively. Although the re-treatment rate for seropositive primary syphilis is consistently higher than the rate for seronegative primary syphilis from the fifth through the twenty-fourth month, at no point is the difference statistically significant.

In Negro males no significant differences are found between stages of syphilis. However, here, as in the white male group, the highest rate is found in the secondary stage, the lowest in the seronegative primary stage, from the twelfth through the twenty-fourth month of posttreatment observation. The re-treatment rates vary from 16.2 percent for seronegative primary to 19.1 percent for secondary syphilis at the twelfth month, and from 18.9 percent for seronegative primary to 26.2 percent for secondary syphilis at the twenty-fourth month.

In the section of Chart 1 devoted to Negro females, the curve for seronegative primary syphilis has been omitted because of the small number of cases (28 observed for 2 years). Although the differences are not as striking as in the white male group, secondary syphilis in the Negro female has a higher re-treatment rate than seropositive primary syphilis from the eighth through the twenty-fourth month. It is significantly greater[3] from the fifteenth through the twenty-fourth month of posttreatment observation.

Chart 2 is a comparison of results of therapy by race and sex. The re-treatment rates for Negro males are more than double the rates for white males with seronegative primary syphilis from the seventh through the twenty-fourth month of posttreatment observation.[2] Approximately the same difference exists in seropositive primary as in seronegative primary syphilis between the re-treatment curves for white males and Negro males. The differences in rates are statistically significant[2] from the sixth through the twenty-fourth month of posttreatment observation. The cumulative re-treatment curve for Negro females falls about midway between the curves for white males and Negro males.

In secondary syphilis, the only stage in which comparisons can be made for all four race-sex groups, the differences in re-treatment rates practically disappear. Although the re-treatment rates for Negro females are slightly lower than the rates for the other 3 race-sex groups from the sixth through the eleventh month, this difference is eliminated during the second year of posttreatment observation.

These observations may be summarized as follows:

1. In white male patients the cumulative re-treatment rate for secondary syphilis is from 2 to 3 times the rates observed in seronegative and seropositive primary syphilis from the seventh through the twenty-fourth month of posttreatment observation.
2. In Negro males no significant differences are found in re-treatment rates between the stages of syphilis.
3. In both seronegative and seropositive primary syphilis, the cumulative re-treatment rate in Negro males is about double the cumulative rate in white males from the seventh through the twenty-fourth month of posttreatment observation.
4. No significant differences are observed between the 4 race-sex groups in patients treated for secondary syphilis.

As stated previously, these findings are based on an over-all analysis of the 6,310 cases included in the study. In order to determine whether the results have been influenced by an uneven distribution of

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[2] Statistically significant either the 1-percent or 5-percent level throughout period specified.

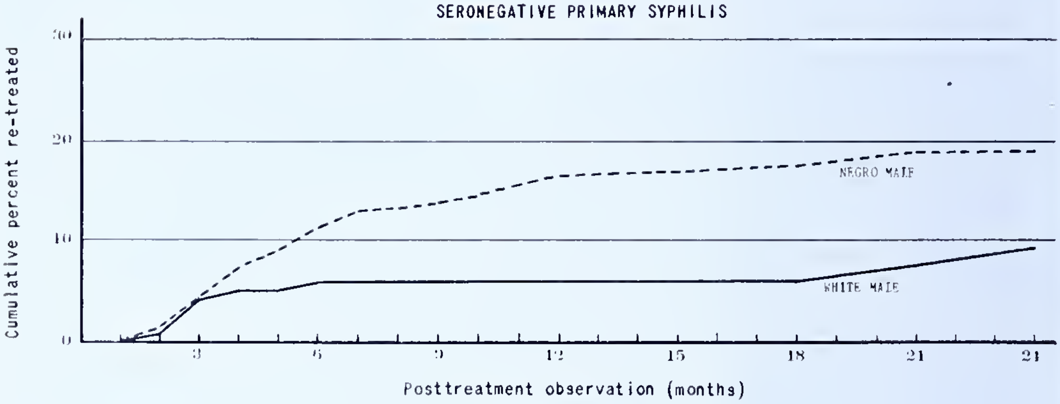
[3] Statistically significant at the 5-percent level.

CHART 2

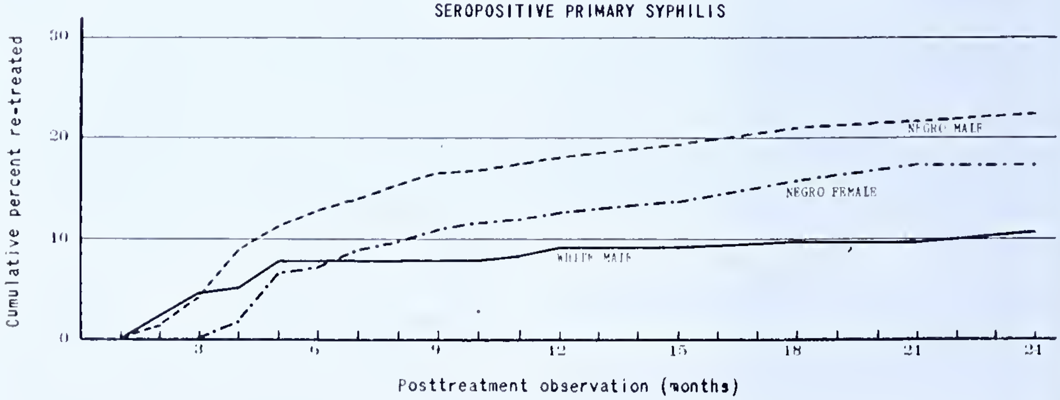
INFLUENCE OF RACE AND SEX ON RESULTS OF THERAPY FOR EARLY SYPHILIS

TOTAL OF ALL SCHEDULES OF THERAPY

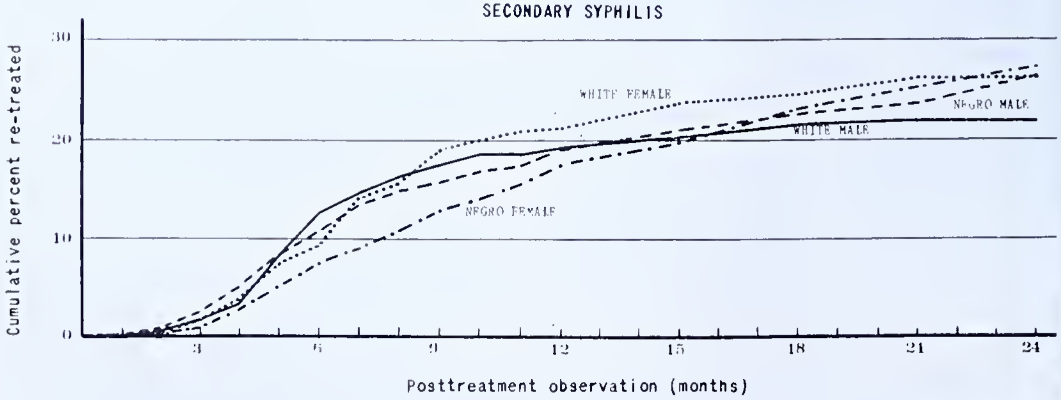
SERONEGATIVE PRIMARY SYPHILIS



SEROPOSITIVE PRIMARY SYPHILIS



SECONDARY SYPHILIS



cases by schedule of therapy, analyses of variance by schedule of therapy have been done. For those who are interested, the re-treatment rates upon which the analyses are based and the results of the analyses are presented in the appendix.

These analyses of variance not only confirm the findings in the over-all analysis, but eliminate schedules of therapy as the factor responsible for the differences or similarities observed between races, sexes, and stages of syphilis.

It is interesting to speculate on a possible explanation for these apparent differences in results of therapy. If there were a true difference in response to therapy between the races, this difference would be maintained throughout the early stages of the disease. As demonstrated, however, Negro males have a higher re-treatment rate in the two primary stages of the disease, but in the secondary stage the rates for Negro males and white males are more in harmony. A more logical explanation for the differences between the white and Negro races would be the greater amount of reinfection in the Negro, because of the higher incidence of syphilis in the Negro race.

If the difference between races is attributable to reinfections, the following conclusions may be drawn:

1. Since in both seronegative and seropositive primary syphilis the re-treatment rates at the end of 2 years of posttreatment observation in Negro males are more than double the rates in white males, the bulk of "re-treatments," at least in the Negro race, in the primary stages of syphilis are actually reinfections rather than treatment failures.
2. Reinfections play a much less important role in secondary syphilis, as evidenced by the similarity of rates between white and Negro males (21.8 and 26.2 percent).

This suggestion regarding higher reinfection rates in primary syphilis is strengthened by a recent article by Magnuson (2). He has demonstrated in rabbits that following infection "There is a progressive development of the acquired immunity throughout the first 24 weeks. . . . By the end of 12 or 24 weeks the animal is completely immune to the reinoculation of several thousand times the original infecting dose, and fails to develop symptomatic reinfection even when 10,000,000 times the original infectious dose is inoculated." These data are translated, with reservations, to syphilis in man, with the conclusion that patients treated early will have a preponderance of symptomatic reinfections; those treated in the secondary stage may be expected to have more asymptomatic reinfections, which will be clinically manifest (if at all) by "serologic relapse" and neither symptomatic nor asymptomatic reinfection will be of importance in those treated late in the disease.

On the basis of the foregoing discussion, it would appear that the "re-treatment" rates more nearly represent the true "failure" rates in secondary syphilis than they do in primary syphilis. For this reason, as well as for the fact that results of therapy in secondary syphilis are least affected by the factors of race and sex, it is felt that the secondary stage of the disease furnishes the best basis for comparison of the effectiveness of various types of therapy for early syphilis. All of these factors should be kept in mind in reviewing and comparing the treatment results that have been reported in the literature.

Appendix

Analyses of Variance by Schedule of Therapy

Because of the large number of schedules employed in the two centers, it has been necessary to group them as follows:

A. 600,000 units of penicillin—10,000 units q 3 hours for 8 days.

B. 1,200,000 units of penicillin (duration 4, 8, and 15 days).

C. 1,200,000 units of penicillin—20,000 units q 3 hours for 8 days plus 320 mg. of arsenoxide.

D. 2,400,000 units of penicillin (duration 8 days, 2- or 3-hour interval between injections).

E. 2,400,000 units of penicillin—40,000 units q 3 hours for 8 days plus 320 mg. of arsenoxide and 600 mg. of bismuth.

F. 1,200,000 or 2,400,000 units of penicillin in 8 days plus 3 sessions of fever of 3 hours each.

G. 1,200,000 or 2,400,000 units of penicillin in 28–30 hours plus one 6-hour session of fever.

H. 4,800,000 units of penicillin in aqueous solution (8 days' duration, 2- or 3-hour interval between injections).

I. 4,800,000 units of penicillin in oil and beeswax in 8 days or 5,000,000 units of penicillin in oil and beeswax in 10 days.

J. 10,000,000 to 25,000,000 units of penicillin by 1-day intravenous drip.

K. One-day fever therapy: temperature maintained at 105°–106° for 6–8 hours; 150 mg. of bismuth, and 1.7 or more mg. of arsenoxide per kg. of body weight, or a total of 120 mg.

L. Schoch.

Analyses of variance are based on the cumulative re-treatment rates at the 12- to 15-month observation period. This selection was made not only because it is felt that the differences observed at this point are representative of the 24 months of observation, but also because inclusion of a greater number of schedules is made possible since more patients are observed for 15 months than for 2 years. Re-treatment rates are based on a minimum of 10 patients observed for this period of time. Because of such small totals, the arc-sin transformation has been employed.

The first analysis of variance compares the re-treatment rates of primary and secondary syphilis for white males (table 2). Eight of the 12 schedules listed are included. The stage of syphilis at the time treatment is administered to white male patients is a definite factor in the results obtained. (The F value is 13.27; the least significant values are 5.59 at the 5-percent level and 12.25 at the 1-percent level.)

Table 2.—*Cumulative re-treatment rates (percent) for white males by stage of syphilis and schedule of therapy*

Schedule	Primary syphilis	Secondary syphilis
A	16. 8	40. 0
B	6. 3	22. 0
C	3. 5	13. 2
D	10. 4	11. 4
E	0	20. 3
H	0	0
I	2. 9	13. 2
J	40. 9	85. 8

The second analysis of variance, based upon cumulative re-treatment rates as presented in table 3, is for Negro males by stage of syphilis and includes 11 of the 12 schedules listed. As in the overall analysis, no significant difference is found between the stages of syphilis. (The F value is 1.03, and the least significant value at the 5-percent level is 3.49.)

Table 3.—*Cumulative re-treatment rates (percent) for Negro males by stage of race, sex, and schedule of therapy*

Schedule	Seronegative primary	Seropositive primary	Secondary syphilis
A	19. 5	26. 1	31. 2
B	19. 3	19. 9	23. 1
C	27. 7	17. 3	15. 9
D	12. 3	13. 5	14. 2
E	10. 5	13. 1	11. 3
F	30. 3	30. 0	4. 5
G	22. 2	29. 9	33. 3
H	4. 5	15. 7	14. 6
I	10. 2	15. 0	13. 7
J	32. 4	38. 3	53. 8
K	11. 1	23. 7	26. 1

The third analysis includes both seronegative and seropositive primary syphilis and compares the results of therapy in white males and Negro males. As shown in table 4, 8 of the 12 schedules are included. This analysis substantiates the observation that in primary syphilis Negro males have a higher re-treatment rate than white males. (The F value is 12.20; the least significant values are 5.59 at the 5-percent level and 12.25 at the 1-percent level.)

The fourth and last analysis of variance, based on the cumulative re-treatment rates for secondary syphilis as presented in table 5, includes all 4 race-sex groups and eight schedules of therapy.

Little or no difference in results of therapy exists between races and sexes in the secondary stage of syphilis. (The F value is 4.03, with 8.66 as the least significant value at the 5-percent level.)

Table 4.—*Cumulative re-treatment rates (percent) for white males and Negro males treated for primary syphilis by schedule of therapy*

Schedule	White male	Negro male
A	16.8	23.4
B	6.3	19.6
C	3.5	20.2
D	10.4	13.0
E	0	11.8
H	0	11.6
I	2.9	13.3
J	40.9	35.7

Table 5.—*Cumulative re-treatment rates (percent) for secondary syphilis by race, sex, and schedule of therapy*

Schedule	White male	White female	Negro male	Negro female
A	40.0	48.1	31.2	28.6
B	22.0	34.9	23.1	21.5
C	13.2	18.7	15.9	17.7
D	11.4	15.5	14.2	19.8
E	20.3	10.0	11.3	11.8
H	0	0	14.6	16.6
I	13.2	18.0	13.7	15.8
K	26.5	25.5	26.1	20.6

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Asexual Syphilis in Children [1]

Henry Eisenberg, Surgeon (R), United States Public Health Service;
Frederick Plotke, M. D., M. P. H.; and Amelia H. Baker, M. A.

It is generally conceded that the number of asexual contacts of infectious syphilis who actually develop syphilis is small in relation to the total new infections each year. Such contacts are usually familial, and infected adults in families seem to be the most frequent source of infection to children.

Very little information concerning this type of transmission can be obtained from the recent literature. A survey was conducted over a period of 1 year in one of the clinics of the Venereal Disease Control Program, Chicago Health Department, to investigate this problem. It is the purpose of this paper to show that the incidence rate of asexually acquired syphilis in children is much higher than ever before suspected.

Although Stokes (*1*) states that "while uncommon, it is by no means a rare occurrence," not much information of recent reference on asexual syphilis infections can be found in his or in Moore's (*2*) latest book.

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[1] From the Municipal Social Hygiene Clinic, Venereal Disease Control Program, Chicago Health Department, in cooperation with the United States Public Health Service. Under the direction of Herman N. Bundesen, Senior Surgeon (R) (Inactive) U. S. Public Health Service; President, Chicago Board of Health.

Smith, Jr., (*3*) reviewed the literature in 1939 on the problem of acquired syphilis in children. In his series of 125 cases covering a period of 17 years and collected from many different clinics, 45 of them occurred in children under 10 years of age. He attempted to arrive at an incidence rate by comparing acquired syphilis in children with early acquired syphilis in adults, and found that the ratio was one to 100. Dyar and Goodwin (*4*) in 1941 added 19 more cases to the literature, of which 8 were under 10 years of age, but did not give any incidence rate. If the incidence is higher than 1 percent, as reported by Smith, Jr., then it is our belief that the possibility of this mode of transmission should assume greater importance to the physician and epidemiologist alike.

The material reported here was collected at the Municipal Social Hygiene Clinic of the Venereal Disease Control Program, Chicago Health Department, during the year 1947. It consists of 20 cases of asexually acquired infectious syphilis in children under 10 years of age and includes all cases so diagnosed in the clinic during 1947. The upper age limit of 10 years of age was chosen because sexual promiscuity is more apt to be present in the young adolescent; consequently, it is much more difficult to determine whether contacts were sexual or asexual after 10 years of age. These children were all exposed to an adult in the household or family who had early infectious syphilis. Four patients were male, 16 were female, and the average age was below 5. Of these 20 cases, 16 have no relationship to each other and the remaining 4 were siblings of two families.

In all cases a thorough investigation was made, with complete histories as to blood serologies at birth, in order to exclude congenital syphilis. Sixteen cases, or 80 percent, were females. During their physical examinations, particular emphasis was laid upon the examination of the vagina in order to exclude the vaginal route of infection. No indication of sex play was found in any of these 16 cases. Several of the children were brought to the clinic by members of the family because of an exanthema. The larger proportion of cases, however, was found as the result of contact interviewing by epidemiologists who took great pains in obtaining familial contacts as well as sexual contacts in adults with early infectious syphilis, where the living conditions were believed to be such that the exposure of children in the household was a reasonable possibility. These children were given repeated general physical examinations and serologies for 3 months.

All cases of infectious syphilis seen at the Municipal Social Hygiene Clinic are sent directly to the Chicago Intensive Treatment Center. During the year 1947, 721 of these patients were diagnosed as having secondary syphilis. There were 20 cases under 10 years of age diagnosed as secondary syphilis in which it was determined that they were familial or asexual contacts. This would give an incidence rate of 2.8 percent of reported acquired asexual syphilis in children.

In comparing the ratio reported by Smith, Jr., (*3*) with that found in our clinic, it is 180 percent higher in our study. We included only syphilis asexually acquired through familial contacts and did not count syphilis acquired by either attempted sexual intercourse, rape, transfusion, or unknown data, as was done by Smith.

A few examples of the asexual infections are hereby presented. The patients' names are fictitious.

Case Reports

History 1

Mary Black, female, colored, married, aged 24 years, was first seen in the Municipal Social Hygiene Clinic during February 1947. The patient had a papular rash on the face, arms, palms of her hands, and soles of her feet. The darkfield examination was positive. A diagnosis of secondary syphilis was made.

Two of her children, Jane, 2 years of age, and Dora, 3 years of age, were examined after the mother was diagnosed, and both were found to be negative. Two months later, Jane was reexamined. Secondary lesions were present, darkfield was positive, and blood test (Kahn) was 320 units. A diagnosis of secondary syphilis was made. Dora, at the time her sister was diagnosed, showed no clinical symptoms of syphilis and the blood test (Kahn) was negative. Three months later, this child was found to have a generalized maculopapular eruption. Darkfield was negative, but the blood test (Kahn) was 40 units, and a diagnosis of secondary syphilis was made. It appears in this case that the mother infected the 2-year-old Jane, and that Jane, who slept in the same bed with her 3-year-old sister, Dora, subsequently infected her.

History 2

Jane Doe, female, colored, married, 18 years of age, was seen in the Municipal Social Hygiene Clinic in June 1947. A large, round, indurated lesion was found on the right nipple. Darkfield was positive, and the blood test (Kahn) was 40 units. A diagnosis of primary syphilis was made. This patient's child, Edith, 11 months of age, was breast fed, and was examined on the following day and found to have moist papules of several weeks' duration over the arms, legs, and trunk. The darkfield was positive; blood test (Kahn) was 400 units. A diagnosis of secondary syphilis was made.

Epidemiologic investigation revealed that Jane Doe's 15-year-old sister, Mary Smith, had been diagnosed as a highly infectious case of secondary syphilis 4½ months prior, and that Mary Smith had been a frequent visitor to the home of her sister, had taken care of the baby, and had habitually fondled her. It was, therefore, concluded that the baby was infected by her 15-year-old aunt, and that the baby, in turn, infected her mother during the nursing process.

History 3

Polly Gaye, colored, female, married, 43 years of age, was diagnosed as having secondary syphilis in April 1947. At that time she had a rash covering her face, body, and palms of her hands and had mucous patches in the mouth. Darkfield was positive; blood test (Kahn) was 80 units.

A married daughter and her husband, who lived in the household, and their eight children, ranging in age from 3 months to 12 years, were examined and all were found to be negative. Four months later, a grandchild, Lucy Gaye, 10 years of age, was discovered to have a rash covering the body. Darkfield was negative; blood test (Kahn) was 360 units. A diagnosis of secondary syphilis was made.

Another grandchild of Polly, Henry Gaye, 7 years of age, showed a fading rash. Darkfield was negative; blood serology was 80 units. A diagnosis of secondary syphilis was made.

It is believed that these children were infected asexually by the grandmother, who frequently slept in the same bed with the children.

History 4

Ruth Hale, colored, 16 years of age, was first seen in a health department clinic in Mississippi in May 1947, at which time a diagnosis of secondary syphilis was made. Her younger sister, Alta, 7 years of age, was examined in one of our clinics 3 months later. She had a papular rash covering the body, genitalia, and face. Darkfield was positive, blood test (Kahn) was 360 units, and a diagnosis of secondary syphilis was made.

It appeared from epidemiologic investigation that the 7-year-old child had very likely acquired syphilis through asexual contact with the older sister, since they slept in the same bed and since there was no evidence of sexual experience.

History 5

Ula Norris, colored, female, 34 years of age, was seen in our clinic in July 1947, with a maculopapular rash covering the entire body. Mucous patches were present in her mouth, darkfield was positive, and blood test (Kahn) was 120 units. A diagnosis of secondary syphilis was made.

Her daughter, Julia, 2 years of age, was examined 6 weeks later. She had a rash around the lower part of the abdomen, including the genitalia, arms, and legs.

Darkfield was negative; blood test (Kahn) was 360 units. A diagnosis of secondary syphilis was made. The mother at the time of delivery had had a negative serology, and the child had shown no symptoms of congenital syphilis at the time of birth. It is, therefore, assumed that the mother infected her child.

It should be noted that in one of the cases cited, an extragenital chancre was acquired asexually on her nipple by a mother from her infected infant. Tucker and Mulherin (*5*) list five chancres on the nipple in a survey of 219 extragenital chancres. They also report on 22 children in whom extragenital chancres were found; however, in only seven cases did they feel that the mode of transmission was apparently made possible by sleeping with an infectious syphilitic person.

An important observation in our series of cases was the fact that in none of our 20 children was a primary lesion found. It is possible that the chancre was so small in size and was so situated that it was overlooked by the parent and that it had disappeared before the child was brought to the clinics. The reports by Smith (*3*), as well as Tucker and Mulherin (*5*), seem to confirm the belief that extragenital chancres in children are smaller than those seen in adults. All our cases showed a generalized maculopapular rash of secondary syphilis.

Intimate contacts in overcrowded households with poor standards of personal hygiene seem to play an important part in asexual transmission of syphilis to children. It would appear to be the responsibility of the doctor and of the epidemiologist to place more emphasis on familial investigation. All children belonging to a household where an infectious syphilis patient, particularly one with a secondary eruption, has been living should be examined frequently. They should be given repeated serologic tests for syphilis for three months from the last date of exposure. The risk of an innocent infection with syphilis is apparent and the possibility of such transmission should be emphasized to the patient. Infected persons should be instructed as to proper hygienic precautions in order to protect other members of the household. Greater efforts of doctors and epidemiologists directed toward education and complete investigation with regard to familial contacts should decrease the incidence rate of asexually acquired syphilis in children.

Summary

1. The Municipal Social Hygiene Clinic of the Venereal Disease Control Program, Chicago Health Department, reports 20 cases of asexually acquired syphilis in children under 10 years of age.

2. Among this group of 20 children, there were 16 female and 4 male children. The average age was below 5 years; 4 children were siblings from two different families.

3. This report covers all cases diagnosed during the year 1947. In comparing all cases diagnosed as secondary syphilis with those acquired asexually in children under 10 years of age, the incidence is 2.8 percent.

4. In all cases one member of the household or family in a close relationship with the child had been diagnosed as having secondary syphilis.

5. None of the 20 infected children showed a primary lesion upon examination in the clinic; 15 children, or 75 percent, had positive darkfields upon first examination, while all 20 had positive serologies.

6. Overcrowded home conditions and lack of education in hygienic matters appear to be conducive to acquiring syphilis asexually among children exposed to infectious syphilis.

7. Children in families where a member is diagnosed as having early infectious syphilis should be followed for 3 months from the last date of exposure.

8. Education of the patient by the clinician and the epidemiologist should reduce this type of infection.

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Comparative Studies on Mailed Spinal Fluid Specimens[1]

George R. Cannefax, Bacteriologist; George E. Parkhurst, Senior Surgeon; and Richard W. Bowman, Biostatistician, United States Public Health Service

Observations by the medical officers during the past 5 years at the Hot Springs Medical Center, Hot Springs, Arkansas, have indicated that follow-up spinal fluid specimens received by mail frequently showed total protein and Kolmer test results to be higher than the results obtained on the same patient while under treatment at the Medical Center.

Subsequent referral to the Medical Center of several of these patients for complete spinal fluid recheck and possible retreatment showed total protein and Kolmer test results to be comparable (or nearer normal) to the spinal fluid findings obtained during the patients' original stay at the Medical Center. Such an elevation in test results for total protein and Kolmer titer on spinal fluid follow-up specimens *mailed* to the Medical Center laboratory was cause for considerable question, and further suggested that the frequently elevated test results on mailed specimens (as judged in comparison to the original spinal fluid findings while the patient was at the Medical Center for treatment) might possibly be interpreted as "*falsely*" elevated spinal fluid total protein and Kolmer values.

A review of these observations suggested the possibility that similar conditions might exist for other spinal fluid specimens *mailed* to the Medical Center laboratory for examination. The significance of this suggestion is emphasized when one considers a diagnosis of asymptomatic neurosyphilis substantiated by elevated total protein and Kolmer test results on a specimen mailed to the laboratory from an outside source. The above considerations served as the stimulus for conducting this study.

From March 1 to April 15, 1948, a study was conducted at the Hot Springs Medical Center in order to determine the extent and degree of variation in spinal fluid findings that might exist between (1) a portion of the identical spinal fluid specimen tested within 2 hours after collection from the patient and (2) specimens mailed to the laboratory from outlying areas within the State at a later period of time.

The spinal fluid was removed from each patient by cisternal puncture, using a sterile 10 ml. syringe and needle. The needle used for withdrawing the spinal fluid was immediately removed from the syringe and replaced by a second sterile needle before the fluid was transferred to the test tubes. Merthiolate was not used in any tube containing spinal fluid specimens. Each spinal fluid specimen was divided in 3 parts and each part was placed in a separate test tube.

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[1] From the U. S. Public Health Service Medical Center, Hot Springs National Park, Ark.; George E. Parkhurst, Medical Officer in Charge; George R. Cannefax, Laboratory Director.

1. The first portion of each specimen was placed in a tube which had been cleaned and sterilized in a hot air sterilizer, with no effort being made to maintain sterility after the tube was removed from the sterilizer. The tube was not closed during the short interval before testing. This was identified as the control portion of the specimen.

2. The second portion of each specimen was introduced into a sterile, rubber-stoppered, vacuum-sealed tube. This was identified as the Vacutainer portion of the specimen.

3. The third portion of each specimen was placed in a tube prepared in the same manner as the control specimen, but a nonsterile cork stopper was used to close this tube after spinal fluid had been injected into it. This was identified as the cork-stoppered portion of the specimen.

The control portion of the specimen was held at room temperature and was tested within 2 hours after collection. The Vacutainer and cork-stoppered portions were held at room temperature at the laboratory for a period of 1 to 7 days before being carried by station wagon to a distant point in the State and mailed back to the laboratory. The interval between collection and testing of the mailed portions of the specimens varied from 2 to 9 days.

This study is based on 106 cisternal spinal fluid specimens. These 106 specimens are a random sample and include diagnoses of early syphilis, early latent syphilis, late syphilis, and neurosyphilis. In table 1, these cases are presented showing a comparison of normal and abnormal protein content in the mailed and control portions of spinal fluid. Any total protein estimation above 24.0 mg. percent was considered abnormal. A Klett-Summerson photoelectric comparator was used for the quantitative estimation of total protein for all specimens.

In the control portion of the specimens (tested within 2 hours after collection), 19 (17.9 percent) of the 106 cases showed abnormal protein content. In the portions mailed in Vacutainers, 24 (22.6 percent) of the 106 cases were abnormal, while in the portions mailed in cork-stoppered tubes, 63 (59.4 percent) of the 106 cases showed abnormal findings.

In table 2, the average total protein in the mailed portion of the specimens is compared by various time intervals between collection and testing with the corresponding control portion of the specimens, which were tested within 2 hours after collection. The elevation in total protein content observed in the mailed portions at 2 to 4 days did not tend to increase further in the interval 5 to 6 days or 7 to 9 days. In the total group it is found that the average increase in total protein in the Vacutainer portion of the specimens is 13.4 percent, while the average increase in the cork-stoppered portion is 54.3 percent. The percentage of mailed specimens in which increases in total protein were found was 87.7 for Vacutainers and 96.2 for cork-stoppered containers.

Table 3 shows the results of the Kolmer complement-fixation test on the control portion of the specimens tested within 2 hours after collection compared with the corresponding portions mailed at later periods. In this table a weakly positive Kolmer includes tests with a positivity of 1+, 2+, or 3+ in the first dilution (.5 cc.); moderately or strongly positive includes those cases with a positivity of 4+ in the first and subsequent dilutions. The Kolmer test on the Vacutainer portion of the specimens most nearly agreed with the control portion. There were 3 cases which showed a positive Kolmer in the Vacutainer portion of the specimens that were negative in the corresponding control. Of the 12 cases with a positive Kolmer in the control portion, 10 showed less positivity in the Vacutainer portion (in most instances a variation of 1 dilution), and 2 showed the same degree of positivity. Anticomplementary Kolmer results were obtained from turbid specimens which were ob-

Table 1.—*Comparison of normal and abnormal protein content in mailed and control portions of specimens of spinal fluid*

Type of specimens	Normal protein content		Abnormal protein content		Total	
	Number	Percent of total	Number	Percent of total	Number	Percent of total
Mailed portions:						
Vacutainer	82	77.4	24	22.6	106	100.0
Cork-stoppered container	43	40.6	63	59.4	106	100.0
Control portion	87	82.1	19	17.9	106	100.0

Table 2.—*Percentage of increase in total protein content of mailed portion of the spinal fluid specimens over control portion of the specimens*

Interval between collection and testing of mailed portions of the specimens	Number of specimens	Mailed portion of the specimens				Control portion of the specimens [1]
		Vacutainer		Cork-stoppered container		
		Average protein content (mg. percent)	Percent increase	Average protein content (mg. percent)	Percent increase	Average protein content (mg. percent)
2–4 days	30	20.7	16.9	27.8	57.1	17.7
5–6 days	50	20.9	10.6	27.8	47.1	18.9
7–9 days	26	22.2	16.8	31.2	64.2	19.0
Total	106	21.1	13.4	28.7	54.3	18.6

[1] All control portions of the specimens were examined for protein content within 2 hours from their time of collection; they are listed at the end of the table to correspond to the mailed portions for each group for the purpose of easy comparison.

Table 3.—*Percentage distribution of results of Kolmer complement-fixation test on mailed and control portions of the specimens of spinal fluid*

Interval between collection and testing of mailed portions of the specimens	Number of specimens	Mailed portion of the specimens							Control portion of the specimens [1]		
		Vacutainer			Cork-stoppered container						
		Moderately or strongly positive	Weakly positive	Negative	Moderately or strongly positive	Weakly positive	Negative	Anticomplementary	Moderately or strongly positive	Weakly positive	Negative
2–4 days	30	3.3	3.3	93.3	30.0	13.3	40.0	16.7	0.0	0.0	100.0
5–6 days	50	10.0	2.0	88.0	38.0	16.0	46.0	0.0	12.0	2.0	86.0
7–9 days	26	11.5	7.7	80.8	42.4	3.8	50.0	3.8	19.2	0.0	80.8
Total	106	8.5	3.8	87.7	36.8	12.2	45.3	5.7	10.4	0.9	88.7

[1] All control portions of the specimens were tested by the Kolmer technic within 2 hours from their time of collection; they are listed at the end of the table to correspond to the mailed portions for each group for the purpose of easy comparison.

served only in cork-stoppered tubes. Fifty-two (49.0 percent) of the specimens mailed in cork-stoppered containers showed positivity in the Kolmer test (36.8 percent moderately or strongly positive and 12.2 percent weakly positive) as compared with 12 (11.3 percent) of the corresponding controls.

In comparing the results of the mastic test, the readings in the first 5 tubes were summed and the case grouped according to the total. For example, a specimen showing a mastic reading of "443221000" would be classified as "15." The only difference in results of the mastic test between the mailed portion of the specimens and the control portion was the slight precipitation in the first and second tubes of the Vacutainer and cork-stoppered portions of the specimens (table 4).

In all tests made on the spinal fluid, the results from cork-stoppered containers showed a statistically significant difference from the control portion and, in general, from the portion mailed in the Vacutainer.

Table 4.—***Percentage distribution of results of mastic test on mailed and control portions of the spinal fluid specimens***

Sum of readings in first 5 tubes of mastic test	Mailed portions of the specimens				Control portion of the specimens	
	Vacutainer		Cork-stoppered container			
	Number	Percent of total	Number	Percent of total	Number	Percent of total
0	53	50.0	56	52.8	85	80.2
1–4	44	41.5	41	38.7	13	12.2
5–10	3	2.8	2	1.9	2	1.9
11–25	6	5.7	7	6.6	6	5.7
Total specimens	106	100.0	106	100.0	106	100.0

This study shows that the laboratory results on specimens mailed in nonsterile containers frequently do not present a true picture of the spinal fluid findings. This might suggest that an undetermined number of people who have been diagnosed asymptomatic neurosyphilis and started on treatment may not have neurosyphilis at all, but that their spinal fluid specimens were mailed in nonsterile containers with an accompanying lapse in time prior to examination, and either the Kolmer showed a "false" positive or the total protein estimation went above the maximum of normality for the laboratory performing the test.

It is suggested that similar studies be conducted in an effort to establish a sound basis for handling mailed spinal fluid specimens.

Summary

1. This study demonstrates that the total protein values in spinal fluids are generally higher in mailed specimens as compared with identical specimens tested immediately, and that total protein values show a greater elevation in spinal fluids mailed in nonsterile cork-stoppered tubes than specimens mailed in sterile vacuum-type tubes.

2. Regarding the Kolmer test, this study appears to show that both a short time factor and the use of sterile containers are necessary in order to insure reliable results on mailed spinal fluid specimens. Whereas the control portion of the specimens were 88.7 percent negative and the portion of the specimens mailed in Vacutainers were 87.7 percent negative, the portion mailed in nonsterile cork-stoppered containers were only 45.3 percent negative.

Integration of Public Health Nursing Into a Marine Hospital[1]

J. A. Trautman, Senior Surgeon, and Rosalie Giacomo, Senior Assistant Nurse Officer, United States Public Health Service

Hospitals are giving increased attention to the need for integrating public health methods into their traditional functions of diagnosis and treatment of disease. The Commonwealth Fund's Commission on Hospital Care (*1*) has pointed out the necessity for integration and emphasized the benefits to be gained. The most recent annual census of public health nurses (*2*) disclosed that 133 public health nurses were employed on January 1, 1948, by 106 schools of nursing as instructors and coordinators of public health, a gain of 31 over the previous year.

In the past, hospitals generally confined themselves to the diagnosis and treatment of disease in their patients, with little consideration of the relationship between these patients and the broader aspect of public health. But today many progressive hospitals are recognizing the relationship which exists between the individual afflicted with communicable disease and other members of the community. Many have established programs to integrate their functions with the public health needs of the community, and others are in the process of developing such programs.

The increased interest in integrating public health technics into hospital operations (*3*) (*4*) adds significance to a recent study, conducted at a large marine hospital, to determine the applicability of such integration to an institution serving a selected group of patients, most of whom had their roots outside the community immediately concerned.

Marine hospitals offer all the services usually found in a general hospital, but their patients are confined to the beneficiaries of the United States Public Health Service designated by law. At the United States Marine Hospital, Staten Island, N. Y., where the recent study was conducted, 80 percent of the patients were American merchant seamen, and the remainder came from such groups as the Coast Guard, Engineer Corps, Army Transport Services, Employees' Compensation Commission, immigrants, and alien seamen. Since many of these patients were hospitalized far from their homes and their families, they required more convalescent attention than patients in ordinary hospitals.

For purposes of this study, a public health nurse with a background of experience in local community health work was assigned to the Marine Hospital. The duties ordinarily performed by public health nurses in other hospitals were modified to fit the peculiarities of this kind of institution.

Under the general supervision of the chief nurse and the clinical director, her duties were outlined to include: (1) interviewing patients with venereal diseases, tuberculosis, and other reportable diseases in order to ascertain contacts and other pertinent data; (2) maintaining records of information obtained and assisting in the preparation of appropriate reports to the local health department; (3) acting in a liaison capacity between the hospital and health departments, under the direction of the medical officer in charge, in order that all objectives relative to control and management of reportable diseases might be accomplished; and (4) assisting with the instruction of

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[1] From the U. S. Marine Hospital, Staten Island 4, N. Y. Medical Director: J. F. Mahoney, U. S. Public Health Service.

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nurses in the public health aspects of reportable diseases.

The public health nurse's activities began with the venereal diseases and expanded from there to include tuberculosis and some of the out-patient clinics. During the development of a tumor clinic, she was also called upon to assist in planning a follow-up service to insure the periodic return of patients.

Venereal Disease Program

The venereal disease service, occupying a 60-bed ward, presented immediate integration opportunities. Various intensive therapy schedules were being incorporated into a program which included case finding and education. The chief public health objectives of this service were to educate the patient regarding his disease, to elicit and make disposition of contact information, (5) and to make hospital personnel familiar with public health aspects of venereal diseases.

Education of the patient was started as soon as the patient was admitted to the ward and continued until he was discharged. All teaching content had been carefully checked previously by the medical staff. The learning situation was almost ideal, since motivation in learning about health is intensified when an individual is afflicted. Furthermore, every aspect of hospitalization, whether it is satisfactory or not, constitutes a learning experience. Therefore, the hospital patient gains knowledge whether or not there is a teaching program, but a well-planned program can add tremendously to his health education.

Upon admission to the venereal disease ward, all new patients were informed by the doctor about the movies, lectures, and individual conferences available. Twice a week the public health nurse held group discussions with patients dealing with the causative organisms, modes of transmission, symptoms, course of the diseases, and posttreatment recommendations. A portable exhibit for use during these group conferences was made by cutting pictures of primary, secondary, and late lesions from various journals and attaching them to a white hospital screen. The pictures were mounted on cardboard and pinned to the screen, which could then be easily folded and moved from ward to ward. This illustrated talk was generally held in the ward and was kept informal so that patients would be encouraged to ask questions. Because guilt feelings faded in such a group when the patient saw others about him being treated for the same disease, it was found that group teaching was effective. The material presented was kept flexible enough to appeal to all levels of intelligence. Liberal use of idiomatic and vernacular expressions helped to meet patients on familiar grounds; medical terms, when used, were carefully defined. Early in each group session, it was explained that the purpose of the talk was to increase the patients' knowledge of venereal diseases so that they could help circulate correct information to others who needed advice.

Films were used to supplement the instruction given. The most popular film was a narrative type called "Know for Sure," which is available for loan from most health department film libraries, or from the United States Public Health Service. Leaflets and pamphlets designed for patient education, including literature printed in foreign languages for foreign seamen, were available from a nearby city health department.

Since most of these patients will continue traveling to parts of the world where legalized prostitution appears safe and tempting, the dangers and risks involved in visiting houses of prostitution were pointed out. Many of these patients had never been warned that the so-called "health certificate" displayed in such places offers a false security because negative tests are common during the incubation period and very early stage of syphilis. The men were warned that sex exposure even with protection is not to be considered 100 percent safe. Some time was devoted to pointing out that the successful treatment of one infection does not prevent reinfection. This group interview also prepared the patient to give contact information later in a private interview with the public health nurse.

Following the diagnosis and after attendance at a group discussion, each patient was ready for a private interview with the public health nurse. Psychologically this appeared to be the best time for the nurse to answer personal questions and to obtain certain contact information from the patient. His diagnosis and treatment were reviewed with him before any attempt was made to elicit contacts.

During the private interview, the meaning of the word "contact" as it related to the patients in infectious stages was explained to include all sex partners, male or female, involved from the beginning of the incubation period to the time of treatment. Patients were assured, before being asked for the names of contacts, that such records would be kept confidential and were also told how such records were used in field investigation. When patients wished to make their own arrangements for the examination of contacts, as some did, the resources available in the community were outlined. The patient was encouraged to contribute contact information in the interest of controlling diseases by helping others to secure early treatment. As soon as identifiable contacts were obtained, epidemiological forms were sent to the State department of health, or to the Surgeon General of the United States Public Health Service to be forwarded to the foreign health jurisdictions, if the contact resided out of the continental United States. When a marital partner was involved, arrangements were made for her prompt examination and treatment by the local health department.

Merchant seamen, like other patients, have some emotional shock when they learn their diagnosis, and most of them feel a need for "airing" their problems with someone who has time to listen. A little careful prompting by the interviewer helped to remove certain inhibitions or restraints, thereby permitting frank discussion. For example, a young patient with infectious syphilis neglected to give the doctor pertinent information about himself until he was encouraged to do so by the public health nurse. Fear of censure or punishment had prevented disclosure of some homosexual activities. However, because the subject had been mentioned earlier in an open group conference, the patient sought the public health nurse for advice and was persuaded to see the doctor again regarding his problem. It is well for venereal disease workers to remember that perversion and bisexuality occur at any level of society.

A study of the cause and effect of venereal disease in the occupations of patients treated is valuable. There are obvious reasons why merchant seamen are prone to infections. Their very occupation prevents any normal or regular pattern of living; venereal disease may be merely a symptom of some maladjustment of this enviroment. Many of the local social hygiene activities, especially in the field of education, which reach a great many people, fail to reach this group of men who seldom remain in one community long enough to benefit from it. Greater sexual freedom, which increases the risk of infection, often occurs when the normal restraints of family life are removed.

Liaison Work

An important function of the public health nurse in this study was to keep in close touch with the health department. It was her responsibility to see that all cases were promptly reported to the health department, as required by law, and to supply information pertaining to the location of contacts. The health department worked closely with the hospital in locating patients who failed to report for hospitalization following a preliminary diagnosis in the clinic. Many of the patients returned to tell about satisfactory arrangements made through the health department referrals, for the treatment of wives or other contacts not eligible for care at the Marine Hospital.

Staff Education

Sanitary code regulations pertaining to reportable diseases were discussed with hospital personnel; functions and responsibilities of the health department were also reviewed with all new interns and nurses in order to encourage an appreciation of the work of the local health department. Both interns and nurses were invited to observe group instruction for patients in order to become familiar with the content and to incorporate similar material into their individual instruction of patients.

Interviewing technics were demonstrated and discussed with student nurses, who were encouraged to develop skills along these lines. "An Interviewer's Aid," which can be obtained from the Venereal Disease Educational Institute in Raleigh, North Carolina, is a helpful guide for persons inexperienced in venereal disease interviewing. Another technic useful in teaching students was the development of a manual incorporating all materials used in venereal disease work. The manual contained the sanitary code regulations, hospital policies, copies of all forms used in reporting diseases and contacts, and the location and schedules of all nearby city health department clinics used in referrals.

Tuberculosis Program

Development of the tuberculosis program proceeded along the same lines used in venereal diseases, stressing case finding, case holding, and education. Tuberculosis patients provide a particularly fertile field for education. Experience with them proves again the value of patient education and fosters the conclusion that the "uncooperative" should perhaps be called the "unenlightened."

Group education, in this instance, was not possible because all newly diagnosed tuberculosis patients were isolated and restricted to separate rooms. Education of patients was carried on by means of bedside interviews. Once again literature and materials supplied by various local health agencies were used for patients. The patients were also interviewed to secure names and addresses of close associates who might be either source or spread contacts. Since many of these contacts were cabinmates on a ship, with whom the patient had lived and worked for long periods, many of the shipping companies, in the interest of tuberculosis control, participated in the location and examination of contacts who had no fixed address. Local health agencies also assisted in finding contacts or suspects reported by the hospital. It was the responsibility of the public health nurse to refer those patients who had suspicious X-ray or laboratory findings to out-patient clinics. The nurse was designated as the person through whom information and reports about patients or families were transferred. As in venereal disease, it was also her duty to aid in staff education by interpreting the regulations involved in tuberculosis work.

Other Activities

The public health nurse was used to coordinate medical care of the hospital patient as it related to problems in communicable disease control in the community. This involved meeting all types of individual problems and situations, no two alike.

An example may serve to illustrate the meaning of this function. A boy of 23 came to the hospital to be operated on for appendicitis. His blood serology was positive. Given a repeat test, he again had a positive serology with a moderately high titer. However, the patient denied any extra-marital exposure and said his blood test was negative in the premarital examination. The public health nurse discussed the possibility of premarital experience with him and assisted the boy to recall a stag party which ended in a house of prostitution just prior to his marriage. The nurse explained that he was in the incubation period of syphilis when he was married. The boy was immediately concerned for his wife, who was now 3 months pregnant. Arrangements were made by the public health nurse for the wife to come to the Marine Hospital for a blood test. This gave the nurse an opportunity to make adequate arrangements for the proper medical supervision of pregnancy and treatment for syphilis, which the examination had confirmed.

When necessary, the public health nurse made arrangements with local agencies for the continued care of patients who wished to convalesce at home.

As is usual, time and physical limitations prevented further exploration of projects which should contribute to more comprehensive care of the patient. The year's experience ended with a recommendation from the hospital administrator that the services of the public health nurse be continued; in the future, these services may be extended to patients with cardiac disease, diabetes, and other chronic diseases in which education of the patient is of particular importance.

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Problems in Out-Patient Management of Syphilis in the South[1]

John A. Lewis, Jr., Surgeon, United States Public Health Service[2]

Recent advances in penicillin therapy have made possible the out-patient management of syphilis. There are important reasons why this type of treatment is preferable to in-patient therapy. The chief reason is that the patient can continue employment while he is being treated, and, in addition, he can be treated closer to his residence. The convenience to the patient should increase the percentage of patients willing to take treatment. Another reason is that the cost of out-patient treatment is less than that of hospitalization.

According to present records, there appears to be no serious medical disadvantage to out-patient therapy. One injection of penicillin daily on an out-patient basis for 5 or more days seems to compare favorably with the same treatment on an in-patient basis. Careful evaluation should be made, however, to be certain that new factors introduced into the reckoning do not influence the results. For instance, what effect does the activity of the patient have on the outcome, especially if he is engaged in heavy labor?

The chief problem in out-patient management, especially in the South, is to find physicians and nurses to provide the treatment. In certain localities, the shortage of local health officers and nurses is so great that even existing services are threatened. During the first half of this fiscal year (1948), 44,557 patients were admitted to the 10 rapid treatment centers in District 4; of these, 9,536 were primary and secondary cases of syphilis. Roughly twice that many may be expected to be admitted by the close of the year. The work load for local health agency personnel in the Southern States is already so heavy that it is very difficult to find time to train personnel in new health methods developed as a result of recent scientific advances.

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[1] Presented at the Venereal Disease Seminar (District 1), Amherst, Mass., June 1948.

[2] Venereal Disease Consultant, District No. 4.

In solving the problem of personnel shortages in local health agencies, consideration may be given to using part time clinicians. This is not an encouraging prospect, however, since most physicians in private practice are so busy with their own work that few can spare the time.

There are some problems that arise in connection with out-patient therapy other than treatment—problems that center around patient education, contact interviewing, suitable clinic and waiting-room space, and the adjustment of clinic hours to fit treatment. Also, the out-patient treatment of syphilis requires more initiative on the part of the patient. He must want treatment enough to make the effort to complete it. Transportation difficulties, misunderstanding as to appointment schedules, illness in his family, recreational interests, and multitudinous distractions are some of the factors which may prevent the patient from reporting as scheduled. His returning to complete the treatment (or his willingness to refer new cases) may depend on whether he likes the service he receives at the local health agency, whether he understands his disease situation, and whether he has a favorable or unfavorable emotional reaction; the clinic should analyze the emotional reaction of the patients to treatment. It is necessary, therefore, that every treatment center pay special attention to its public relations and, in addition, carry on a comprehensive patient education program.

Experience in rapid treatment centers has also shown that patients are good case finders. Many new cases are referred by them. This advantage should not be lost in the conversion to out-patient therapy. In order to be effective in case referral, the patient should have knowledge of the nature of his disease, of the means of its transmission, and of the treatment itself. These things would, of course, be covered in a comprehensive patient education program.

The out-patient facilities must anticipate absorbing the responsibility for patient education and contact interviewing. At rapid treatment centers, personnel have been able to take as much time as necessary to conduct a comprehensive patient education program and to get complete information about contacts; it will not be easy for the clinics to duplicate this good work.

The part that physicians in their private practice can play in converting to out-patient therapy should not be overlooked. Health departments could make information available to physicians on the latest developments in methods of diagnosing and treating venereal diseases and recommended treatment schedules. Since physicians do not usually have time to undertake patient education or contact interviewing, a practical approach might be for health departments to produce a patient education manual which would instruct the patient as to the nature of the disease, the means of its transmission, the importance of reporting each scheduled day, the necessity for total treatment and follow-up tests, and the importance of referring contacts. Physicians use an educational manual in the management of their diabetic patients; a similar manual could be produced for venereal disease patients. We know that these patients are interested in their disease. They are therefore receptive to information about it. A manual would have the possibility of capitalizing on this interest, and the patient could study it at his leisure. It is known that patients often refer contacts for examination: the manual could give the patient his choice of informing the contact of the need for examination and where to get it, or the patient could use the blanks provided to report the contacts. Explanation could be provided that, in the event the blanks are used, investigation would be made by qualified personnel from the health department in a noncensorious and confidential manner. Such a manual is almost a necessity for a busy practitioner to assist him with his responsibilities in patient education and contact investigation. Its success, of course, would depend on the ability of the patient to understand the material presented; it would have little value for individuals who could not understand its contents.

Educational material of this kind could also be used to good advantage in the local health clinics. The fact that approximately 60 percent of the patients treated for syphilis seek treatment of their own volition is indicative that the broad educational work in venereal diseases is catching on. This is indeed encouragement to expand the educational program.

There is also the general problem of the treatment of syphilis which is basic to all management of syphilis everywhere. From time to time we hear that no communicable disease has ever been controlled by treatment methods. From this it is inferred that syphilis cannot be controlled by treatment. If it is true that syphilis cannot be controlled by treatment, there is genuine cause for discouragement. It is important for workers in any field to believe in the essential worth of their work. The work itself must have relevancy to the ultimate goal. There is an obvious fallacy in a statement that venereal disease cannot be controlled by treatment because no other communicable disease has been so controlled. There is in fact no logical connection between the two statements. No comparable effort has ever been made to control any other communicable disease. The doubt arises because there is no certainty of knowledge about the incidence of syphilis. However, every case of venereal disease arises from another case. In addition, we know that treatment interferes with the transmission of venereal disease for varying periods of time. The number of infections which would have arisen if infected individuals had not been treated are the number of cases that are prevented. The problem, then, is to find as many cases as possible that might transmit their infections and to treat them effectively on either an in-patient or an out-patient basis. The more of such cases that are found and treated, the closer we approach the goal of controlling syphilis.

While advances in scientific methods have brought problems of adjustment, the problems are not insuperable. The advantages of simplified treatment with less risk to the patient will have the effect of increasing the percentage of patients treated. Conversion of in-patient to out-patient facilities can take place rapidly where there are well-staffed local health departments. Some areas may have to engage in long-range planning and others must await recruitment of the necessary personnel. Remote areas not justifying a stationary clinic may be served by a revival of the old "blood wagon," which was a traveling clinic that demonstrated its place before the rapid treatment centers came into existence. In any event, it would be helpful to know how the various areas are solving these and similar problems.

The conversion to out-patient facilities can be looked upon as a step in the right direction, bringing us nearer to the ultimate objective of controlling venereal disease.

CURRENT LITERATURE

Note: Abstracts of any article listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

Am. J. Syph., Gonor. & Ven. Dis., St. Louis

- Experimental mouse syphilis. I. Organ distribution of the infectious agent. Paul D. Rosahn, Boris Gueft and Catharine L. Rowe. 32 : 327–336, July 1948.
- Plasma and cerebrospinal fluid iron concentration studies in syphilitic and nonsyphilitic patients. Roger L. Greif. 32 : 337–344, July 1948.
- * Extragenital chancres. A survey of 219 cases. Harold A. Tucker and John L. Mulherin. 32 : 345–364, July 1948.
- False positive serologic tests for syphilis following smallpox vaccination. Theodore Rosenthal and Daniel Widelock. 32 : 365–369, July 1948.
- The Kahn "optimal zone reaction" in seronegative cases of neurosyphilis. Donald Boersma and Phebe G. Williams. 32 : 370–376, July 1948.
- Cardiolipin slide test in the serodiagnosis of syphilis. Sidney J. Klein and George M. Leiby. 32 : 377–390, July 1948.
- Further observations of the electrocardiographic changes in early syphilis. Howard P. Steiger and Joseph Edeiken. 32 : 391–398, July 1948.
- Treatment of neurosyphilis with penicillin alone. Bernhard Dattner. 32 : 399–403, July 1948.

Extragenital chancres. A survey of 219 cases. Harold A. Tucker and John L. Mulherin. Am. J. Syph., Gonor. & Ven. Dis., 32: 345–364, 1948.

The authors have made a survey of 219 cases in an effort to throw light on the characteristic sociologic, racial, and clinical features found in patients with extragenital chancres and to point out some of the sources of diagnostic confusion.

Between 1941 and June 1947, records of 219 patients with extragenital chancres were obtained as follows: 160 from the syphilis clinic of the Johns Hopkins Hospital; 37 from the private practice of Moore and associates; and 22 from the Harriet Lane Home for Invalid Children. In each patient the darkfield examination for *Treponema pallidum*, the serologic test for syphilis, or both, were positive. Over 61 percent of these extragenital chancres occurred in patients between 21 and 40 years of age. The age incidence of genital lesions of primary syphilis in 2,039 clinic patients over the same period of time did not differ significantly from the distribution by age of clinic patients with chancres located elsewhere on the body.

Statistical analyses show a significant preponderance of extragenital chancres occurring in females and in the white race. In both white and Negro patients, lesions of the lip were the most common site of involvement. Chancres in or adjacent to the buccal cavity were found in 69 percent of clinic patients, in 52.5 percent of private patients, and 38.5 percent of children. Multiple extragenital chancres occurred in 15 patients (9.4 percent).

Although immediate sexual contact with infectious lesions of syphilis seemed the most likely explanation for most cases, some chancres were encountered which definitely had not been acquired by sexual contact.

In early literature it was stated that inasmuch as extragenital lesions often followed trauma and because the lips and mouth were especially rich in capillaries and lymphatics, the organisms may have been more deeply placed than usual and the results of treatment in terms of late syphilitic manifestations were worse. Although this may have been an astute clinical observation, the authors show statistically that cases of primary syphilis respond with greater success to treatment than cases of secondary syphilis. Since the majority of those cases with extragenital chancres was in the secondary stage of syphilis, it seems more reasonable to ascribe their adverse therapeutic results to delayed treatment.

Data on general medical performance in the diagnosis of extragenital chancres show that the index of suspicion of syphilis in lesions located elsewhere than the genitals is extremely low.

In conclusion the authors state that any indolent, indurated lesion anywhere on the body, especially if accompanied by unilateral adenopathy, should arouse immediate suspicion of syphilis and that the diagnosis of early syphilis should be a laboratory rather than a clinical procedure.

Arkansas Health Bull., Little Rock

V. D. meeting summarized. 5: 5, July 1948.

Bact. Rev., Baltimore

Characteristics of pathogenic spirochetes and spirochetoses with special reference to the mechanisms of host resistance. Abram B. Stavitsky. 12: 203–255, Sept. 1948.

Bol. Ofic. san panam., Washington

Some international aspects of venereal disease control. Joseph F. Ziemba. 27: 735–740, Aug. 1948.

Brit. M. J., London

Penicillin in the treatment of syphilis. No. 4567: 141–142, July 17, 1948.

Centralized gonococcus culture for dispersed clinics. The value of a new transport medium for gonococci and trichomonas. Mary Moffett, Jean L. Young and R. D. Stuart. No. 4573: 421–424, Aug. 28, 1948.

Bull. U. S. Army M. Dept., Washington

Venereal disease among inductees. Induction policies. Bernard D. Karpinos. 8: 806–820, Oct. 1948.

Canad. J. Pub. Health, Toronto

A comparison of certain serological screen tests employed as aids in the diagnosis of syphilis. Benoit Rousseau. 39: 103–107, Mar. 1948.

Canad. M. A. J., Montreal

Progress in war medicine since 1939. [Syphilis.] L. C. Montgomery. 59: 211–216, Sept. 1948.

Časop. lék. česk., Praha

Současný výskyt progresivni paralysy s obesitou typu Cushingova. Progressive paralysis associated with obesity of the Cushing type. [Neurosyphilis.] O. Skaličkovâ. 86: 72–77, 1947. [Abstracted in Excerpta Med. (Sec. 13—Dermat. & Venereol.), Amsterdam, 2: 55–56, Jan. 1948.]

Chinese M. J., Shanghai

Total nasal reconstruction. The standardized and simplified Indian method. [Syphilis.] Ronald Ru-Yao Sung. 66: 243–246, May 1948.

Urethral diverticulum complicating Neisserian infection. A case report. Yung-Yao Liu. 66: 280, May 1948.

Delaware State M. J., Wilmington

The Wilmington Board of Health and the rapid treatment centers for syphilis. George J. Boines. 20: 30–32, 37–38, Feb. 1948.

Gen. Pract. Clin., Washington

Recent advances in dermatology. Norman Tobias. 5: 197–202, Apr. 1948.

Georgia's Health, Hapeville

Leading diseases in 1947. [Venereal disease.] 28: 1, Aug. 1948.

Know your health department. [Venereal diseases.] 28: 2, Oct. 1948.

Health, Toronto

The Dominion health grants. [Venereal disease.] Health in Parliament. pp. 27, 30, July–Aug. 1948.

War on syphilis. Adrien Plouffe. pp. 16, 31, July–Aug. 1948.

Health News Service, Toronto

VD blood tests said worthwhile. P. 3, Oct. 15, 1948.

Illinois M. J., Oak Park

Pre-marital tests and marriage counseling. 94: 153–154, Sept. 1948.

Indian M. Gaz., Calcutta

Keratosis blennorrhagica. A case report with a review of the literature. Edward W. Gault and Edna I. Gault. 83: 123–125, Mar. 1948.

J. A. M. A., Chicago

Inhalation of penicillin dust. Louis Krasno, Mary Karp and Paul S. Rhoads. 138: 344–348, Oct. 2, 1948.

Clinical problems in penicillin sensitivity. Samuel M. Peck, Sheppard Siegal, Arthur W. Glick and Abner Kurtin. 138: 631–640, Oct. 30, 1948.

Streptomycin in topical therapy. I. Its sensitizing property. Leon Goldman and Milton D. Feldman. 138 : 640–641, Oct. 30, 1948.

Study of 1,000 cases of dementia paralytica. Brazil. Foreign Letters. 138 : 712, Oct. 30, 1948.

J. Bact., Baltimore

Evaluation of precursors for penicillin. G. Kesar Singh and Marvin J. Johnson. 56 : 339–355, Sept. 1948.

J. Clin. Investigation, Cincinnati

The complement content of human sera with especial reference to malaria. [Syphilis.] Anna Dean Dulaney, Jane B. Priest, Mary Lou Almeda and Bii Parker. 27 : 320–326, May 1948. [Part I].

J. Exper. Med., Baltimore

*The antibody response in rabbits to killed suspensions of pathogenic *T. pallidum*. Harry Eagle and Ralph Fleischman. 87 : 369–384, May 1, 1948.

*The rate of bactericidal action of penicillin in vitro as a function of its concentration, and its paradoxically reduced activity at high concentrations against certain organisms. Harry Eagle and A. D. Musselman. 88 : 99–131, July 1, 1948.

The antibody response in rabbits to killed suspensions of pathogenic *T. pallidum.* Harry Eagle and Ralph Fleischman. J. Exper. Med., 87 : 369–384, 1948.

The authors review the literature and report a series of experiments which were undertaken to determine the antibody response in rabbits to killed suspensions of pathogenic *Treponema pallidum*, administered in saline suspension or incorporated in water-in-oil emulsions. Experimental methods, materials and results are presented in detail.

Every one of 37 rabbits injected intravenously with a total of 4.4 to 38 billion dead *T. pallidum* in aqueous suspension developed positive Wassermann or flocculation tests in significantly increased titer. The dilution titers of these tests in the normal series controls varied from 0 to 1 : 4, averaging less than 1 : 2; the titers in the immunized series rose to as high as 1 : 96. The serum dilution titers reached a maximum level within 2 weeks. Thereafter, and despite continuing injection, the titers decreased progressively.

The organisms used in these experiments were derived from rabbit testicula chancres, and the suspensions unavoidably contained tissue extractives. However, the experiments suggest that, a originally postulated by Wassermann, so-called reagin may be simply an antibod to *T. pallidum* which happens to cross-react with alcoholic extracts of mammalian tissue. This is suggested by observations that control animals injecte with extracts of normal testes, either wit or without the addition of nonpathogeni Reiter spirochetes, failed to develop antibodies. Furthermore, it was demonstrated that sedimented organisms containing relatively small amounts of tissu extractives were just as antigenic as th crude chancre emulsion from which the had been concentrated. Methods of preparing treponematal suspensions fro rabbit chancres have not yet yielded suspensions sufficiently concentrated an sufficiently free from tissue component to warrant either their chemical fractionation or their use in absorption experiments, it is stated.

The antiserums did not cause the agglutination of suspensions of pathogenic *T* *pallidum*, living or dead, did not give specific complement fixation with those suspensions, and did not usually cause th living treponemes to lose their infectiousness.

The "immunized" rabbits in the authors' experiments did not regularly develop a significant resistance to infection Intradermal inoculation, in some experiments with as few as 10 living treponemes, regularly resulted in a typica darkfield positive primary lesion at th site of inoculation, whether the animal had been immunized with totals of 3 million organisms intradermally, 53 million organisms subcutaneously, 4.4 t 38 billion organisms intravenously, or 13 to 1,040 million organisms in a water-in-oil emulsion, administered over period which varied from 13 days to 4 months Three of five immunized rabbits whic were challenged by the intratesticular in oculation of 10 organisms failed to develop a primary lesion, while every one of five simultaneously inoculated controls was infected.

The authors discuss the contradiction involved in the production of antibodies cross-reacting with a nonspecific antigen and the nonappearance of specific antibodies against the organism used as antigen.

The rate of bactericidal action of penicillin in vitro as a function of its concentration, and its paradoxically reduced activity at high concentrations against certain organisms. Harry Eagle and A. D. Musselman. J. Exper. Med., 88: 99–131, 1948.

The authors review the literature and report experiments relating to the effect of the concentration of penicillin on the rate of its bactericidal action in vitro against a number of bacteria, including the so-called Reiter strain of cultured *Treponema pallidum*. Methods, materials, and results are described in detail.

The authors observed that the concentration which killed the organisms at a maximal rate was 2 to 20 times the minimal concentration which was effectively bactericidal ("sensitivity" as ordinarily defined); this probably represents the concentration which should be maintained at the focus of infection in order to kill the largest number of organisms in the shortest possible time. Even a 32,000-fold increase beyond this maximally effective concentration did not further increase the rate of bactericidal action of penicillin with some organisms. However, when the concentration of penicillin was increased beyond that optimal level (with approximately half the strains in the authors' studies), the rate at which the organisms died was paradoxically reduced rather than increased, so that the maximal effect was obtainable only within a relatively narrow optimal zone.

The authors observed marked differences between different species of bacteria and occasionally between different strains of the same species, in the maximally effective concentrations of penicillin. Pronounced differences in the maximal rate at which the various bacterial species can be killed by penicillin were also observed. To kill 99.9 percent of the treponemes at the maximally effective level of 1 microgram per cubic centimeter required from 23 to 33 hours, as against 1.4 to 2.2 hours for the C–203 strain of *Streptococcus pyogenes;* the proportion of treponemes surviving after 6 hours was 1 to 10 percent, as compared to 0.002 to 0.01 percent for the streptococcus. These differences in the susceptibility of the bacterial strains to penicillin, in terms of the rate at which they can be killed, may well affect the length of time for which treatment must be continued to effect a cure, it is stated.

It was observed that generally a rough correlation existed between the concentration of penicillin necessary to kill a given organism and the maximum rate at which that organism could be killed by the drug and that within the same bacterial culture, individual organisms also varied in their susceptibility to penicillin. A 4-fold difference in concentration constituted the usual range of variation between the sensitivity thresholds of the most susceptible and the most resistant organisms in a given suspension, it is stated.

J. FLORIDA M. A., JACKSONVILLE

Chronic ulceration of lower leg treated by excision and skin grafting. [Syphilis.] Frederick Hardy Bowen. 35: 152–157, Sept. 1948.

J. IMMUNOL., BALTIMORE

Studies on the interference phenomenon with certain members of the psittacosis-lymphogranuloma group of viruses. Orville J. Golub and John C. Wagner. 59: 59–70, May 1948.

A single-dilution method for the estimation of LD_{50} titers of the psittacosis-LGV group of viruses in chick embryos. Orville J. Golub. 59: 71–82, May 1948.

Some factors influencing the selection of a complement-fixation method. I. A comparison of two quantitative techniques, and an alternative method of expressing serum-dilution titer. Christine E. Rice. 59: 95–107, May 1948.

Studies on lymphogranuloma venereum complement-fixing antigens. IV. Fractionation with organic solvents of antigens of the psittacosis-lymphogranuloma venereum group. Maurice R. Hilleman and Clara Nigg. 59: 349–364, Aug. 1948.

J. INDIANA M. A., INDIANAPOLIS

Infectious mononucleosis—a review of the disease. [VD] William W. Dalton. 41: 1021–1025, Oct. 1948.

J. LAB. & CLIN. MED., ST. LOUIS

Studies on lymphogranuloma venereum: Evaluation of the complement fixation test with lygranum. Morris F. Shaffer and Geoffrey Rake. 32: 1060–1086, Sept. 1947.

J. M. A. GEORGIA, ATLANTA

[Venereal disease.] News items. 37: 241, June 1948.

Legislation for premarital blood tests: the case for and against. Georgia Department of Public Health. Albert Heyman. 37: 322–323, Aug. 1948.

Syphilitic gumma of the aortic ring and left ventricle, and aneurysm of the sinus of Valsalva, with demonstration of *Treponema pallida*. D. F. Mullins, Jr., H. H. Marquis and William Schulze. 37: 340–342, Sept. 1948.

J. M. SOC. NEW JERSEY, ORANGE

Prevention of treatment complications in syphilis with new parenteral multivitamin therapy. Preliminary report. Paul Robert Kline and James J. Colavita. 45: 385–387, Aug. 1948.

Hospitalization of syphilis. Public Health News for the Physician. 45: 464, Sept. 1948.

Treatment of neurosyphilis. Public Health News for the Physician. 45: 464, Sept. 1948.

J. MENT. SC., LONDON

A study of mental derangements in Africans, and an attempt to explain its peculiarities, more especially in relation to the African attitude to life. [Venereal disease.] J. C. Carothers. 93: 548–597, July 1947.

J. ROY. ARMY M. CORPS, LONDON

The early diagnosis of infective hepatitis in syphilitic patients undergoing arsenical therapy. W. Fowler. Clinical and Other Notes. 91: 80–81, Aug. 1948.

J. ROY. INST. PUB. HEALTH & HYG., LONDON

The health of the nation in 1946. [VD] 2: 302–309, Sept. 1948.

J. SOCIAL HYG., NEW YORK

Are we stamping out syphilis? Thomas Parran. 34: 151–157, Apr. 1948.

Social hygiene at the universal military training experimental unit. John M. Devine. 34: 195–200, May 1948.

Venereal disease control in the First Army Area. George J. Carroll. 34: 201–204, May 1948.

Penicillin in the venereal disease control program. Thomas B. Turner. 34: 205–210, May 1948.

WHO expert VD Committee Report is approved. News from the United Nations. World News and Views. 34: 228–232, May 1948.

We're at your service. [V. D.] Philip R. Mather. 34: 308–312, Oct. 1948.

Some social hygiene problems of Los Angeles County. Summary of a report on a community and county-wide survey. Walter Clarke. 34: 313–322, Oct. 1948.

J. SOUTH CAROLINA M. A., FLORENCE

Physiopathological discussion of jaundice in early life. [Syphilis.] M. W. Beach and Clyde D. Conrad. 44: 5–14, Jan. 1948.

Epidermal sensitivity due to streptomycin. George C. Smith. 44: 164–165, May 1948.

*Granuloma inguinale—report of 85 cases treated with streptomycin. Robert J. Zimmermann and George C. Smith. 44: 267–268, Aug. 1948.

Granuloma inguinale—report of 85 cases treated with streptomycin. Robert J Zimmermann and George C. Smith. J. South Carolina M. A., 44: 267–268, 1948.

The authors present an interval report on a series of 85 patients with granuloma inguinale treated with streptomycin at the South Carolina Public Health Hospital. Of this group, 35 were Negro males, 49 were Negro females, and 1 was a white female. Thirty-four patients had coexistent syphilis, and 19 patients displayed positive skin tests for chancroid or lymphogranuloma venereum.

All 3 recognized types of lesions of granuloma inguinale were observed, the most common lesion presented being the ulcerative type, of which there were 37 examples. Prior to admission 52 of the patients had received some form of specific treatment to which they had failed to respond or had developed resistance.

Injections of 0.66 gm. streptomycin in distilled water were given at 4-hour intervals to a total of 20 gm. of the drug. Penicillin-oil-beeswax was also given in those cases wherein secondary infection in the form of fusospirochetosis was present, 400,000 units being given daily for

3 days. All patients with ulcerative or exuberant type lesions were placed on 1:32,000 potassium permanganate sitz baths three times daily to help combat secondary infection.

Symptoms of eighth nerve involvement from the use of streptomycin were observed in 12 cases, but only in 2 cases was the reaction severe enough to indicate cessation of therapy.

Forty-five patients have been observed 1 or 2 months after treatment. Forty of these have been completely healed without further therapy of any kind. Three patients still exhibited small areas of ulceration in the process of healing. One case of streptomycin resistant infection and one case of treatment failure after one course of streptomycin were noted.

A case history is presented of a patient typical of the majority of cases in this series.

J. UROL., BALTIMORE

Clinical observations on the nature of urogenital gonorrhea. John H. Dougherty, Carl S. DiLucia, Angelo DiDonna and John C. Ridder. 57 : 84–93, Jan. 1947.

Synergistic action between the sulfonamides, certain dyes, and streptomycin against gram-negative bacteria : preliminary report. F. S. Thatcher and John T. MacLean. 57 : 902–931, May 1947.

Urological activities of the Navy Medical Corps in World War II. [Venereal disease.] Francis Patton Twinem. 57 : 1129–1134, June 1947.

Male sterility (or impaired fertility). [VD] Edgar A. Slotkin. 60 : 166–175, July 1948.

JOURNAL-LANCET, MINNEAPOLIS

Transactions of the North Dakota State Medical Association. 61st annual session, Jamestown, N. D., May 22–25, 1948. [Venereal disease.] 68 : 346–382, Sept. 1948.

KENTUCKY M. J., BOWLING GREEN

The treatment of syphilis. George Brockman. 46 : 263–269, July 1948.

Eye manifestation of vascular systemic disturbances. Donald J. Lyle. 46 : 287–291, July 1948.

LAB. DIGEST, ST. LOUIS

Modified or improved Pappenheim stain for detection of gonococci in smears. Maxwell M. Barritt. 7 : 12, 1944. [Abstracted in Biol. Abstr., Easton, 22 : 636, Mar. 1948.]

LANCET, LONDON

Cysticercosis cerebri mistaken for cerebral syphilis. Report of a case. A. A. Williams. 2 : 144, July 24, 1948.

Health and disease in 1946. [VD] Ministry's Report. Public Health. 2 : 162–163, July 24, 1948.

M. CLIN. NORTH AMERICA, PHILADELPHIA

Jaundice in the newborn. [Syphilis.] Heyworth M. Sanford. 30 : 75–85, Jan. 1946.

Some unfortunate public health aspects of gonorrhea control. P. S. Pelouze. 30 : 233–238, Jan. 1946.

The treatment of syphilis with penicillin. George X. Schwemlein. 30 : 649–658, May 1946.

The diagnosis and treatment of Reiter's syndrome. Joseph L. Hollander. 30 : 716–723, May 1946.

The diagnosis and management of chronic valvular heart disease. [Syphilis.] William D. Stroud and Morris W. Stroud. 30 : 1301–1306, Nov. 1946.

Present-day methods in the diagnosis of syphilis. Herman Beerman and Norman R. Ingraham, Jr. 30 : 1345–1360, Nov. 1946.

M. J. AUSTRALIA, SYDNEY

A case of arsenical dermatitis successfully treated with BAL. C. C. J. Minty. 2 : 209–211, Aug. 21, 1948.

M. OFFICER, LONDON

Gonorrhoea. Notes and Comments. 80 : 120–121, Sept. 18, 1948.

M. PRESS, LONDON

Various forms of conjunctivitis and their treatment. [Gonorrhea.] R. Lindsay-Rea. Modern Treatment in General Practice. No. 5696 : 7–9, July 7, 1948.

Eye cases in general practice. [Venereal disease.] F. W. G. Smith. No. 5704 : 161–166, Sept. 1, 1948.

MEDICINE, BALTIMORE

Aortic stenosis : a study of the clinical and pathologic aspects of 107 proved cases. [Venereal disease.] Carl William Kumpe and William Bennett Bean. 27 : 139–185, May 1948.

MINNESOTA MED., ST. PAUL

B. A. L. in heavy metal poisoning. Thomas J. Kenyon. Editorial. 31 : 672, June 1948.

A guide for public health nursing agencies seeking to establish policies and standing orders. (June, 1948, Revision—Recommended by the Committee on Public Health Nursing and Approved by the House of Delegates, Minnesota State Medical Association.) [Venereal disease.] 31 : 909–911, Aug. 1948.

Minnesota's Health, Minneapolis

Venereal disease cases decrease. 2 : 4, Aug. 1948.

Nature, London

Venereal disease control in Poland. James Marshall. No. 4105 : 35–36, July 3, 1948.

Rabelais on syphilis. James Marshall. No. 4107 : 118, July 17, 1948.

Nebraska M. J., Lincoln

Gonorrhea in the male—modern management for the general practitioner. Edwin Davis and Leroy William Lee. 33 : 60–63, Feb. 1948.

Considerations concerning gonorrhea in the female. D. C. Vroman. 33 : 64–65, Feb. 1948.

Prostatitis : especially as it relates to cause, treatment and significance. [Venereal disease.] Roy B. Henline. 33 : 266–273, Aug. 1948.

A report of postmortem findings in patients dying in a State mental hospital. [Syphilis.] Frank H. Tanner. 33 : 309–313, Sept. 1948.

Nederl. tijdschr. v. geneesk., Amsterdam

Multiple extragenital primary lesions. H. J. Th. Hiemcke. 1 : Mar. 16, 1945.

New England J. Med., Boston

Alleged penicillin-resistant gonorrhea. Editorials. 239 : 411–413, Sept. 9, 1948.

New York State J. Med., New York

Army venereal disease rate drops as result of new program. 48 : 1141, May 15, 1948.

Penicillin administration via the vagina. Robert I. Walter, Morris A. Goldberger and Louis S. Lapid. 48 : 1159–1161, May 15, 1948.

New Zealand M. J., Wellington

Hepatitis in New Zealand. [Syphilis.] W. M. Porteous. 47 : 201–213, June 1948.

The stability of aqueous solutions, lozenges and creams of penicillin. L. Kirschner. 47 : 214–224, June 1948.

An apparatus for accurate and rapid measurement of penicillin inhibition zones. J. A. Samuel. 47 : 224, June 1948.

North Carolina M. J., Winston–Salem

Granuloma inguinale treated with streptomycin. Report of a case. Sidney Olansky, Joseph Farrington and Kathleen A. Riley. 9 : 21–23, Jan. 1948.

Preventive medicine and voluntary health insurance. [Venereal disease.] Editorial. 9 : 41–42, Jan. 1948.

Paroxysmal cold hemoglominuria. Report of two cases. [Syphilis.] Ralph G. Fleming and Bain L. Heffner. 9 : 142–145, Mar. 1948.

Atabrine in the treatment of trichomonas vaginitis. Fred M. Dula. 9 : 309, June 1948.

Northwest Med., Seattle

Present status of cardiolipin antigen in syphilis serology. William Levin. 47 : 659–662, Sept. 1948.

Idaho State Medical Association. Proceedings of the Fifty-sixth Annual Meeting of Idaho State Medical Association, Sun Valley, Idaho, July 6–8, 1948. [Prostitution.] 47 : 672–680, Sept. 1948.

Oahu Health Council Bull., Honolulu

V. D. rate from prostitution on increase. 3 : 7, Sept. 1948.

Oto-neuro-oftal., Istanbul

Penicillin treatment in ophthalmology. Necdet Sezer. 2 : 30–31, Mar. 1947. [Abstracted in Gen. Pract. Clin., Washington, 5 : 146, Jan. 1948.]

Pennsylvania M. J., Harrisburg

Differential diagnosis of poliomyelitis. [Syphilitic meningitis.] Joseph J. Toland, 3d. 51 : 1205–1208, Aug. 1948.

Policlinico Infantile, Turin

Sui rapporte de lue connatale e sindromi eritroblastiche dei neonati. The relationship between congenital syphilis and erythroblastic syndromes in the newborn. G. Sansone. 1415 : 253–268, 1946. [Abstracted in Excerpta Med. (Sec. 13—Dermat. & Venereol.), Amsterdam, 2 : 51–52, Jan. 1948.]

Post-Grad. M. J., London

Neurosyphilis. A review of recent literature. W. D. Nicol. 24 : 25–30, Jan. 1948.

Reiter's disease. Tendency to ultimate spontaneous cure. R. R. Willcox. 24 : 93–94, Feb. 1948.

Infection in the newborn baby. [Venereal disease.] Alan Moncrieff. 24 : 341–343, July 1948.

Infection in the newborn infant. [Venereal disease.] J. L. Henderson. 24 : 391–406, Aug. 1948.

Presse méd., Paris

Pénicilline et gonococcies (d'après 600 observations recueillies à Lille). Les debuts de la pénicilline-résistance. Penicillin and gonococcal infections (the results of 600 cases seen at Lille). The beginning of penicillin-resistance. C. Huriez and M. Desurmont. 55 : 13–14, 1947. [Abstracted in Excerpta Med. (Sec. 13—Dermat. & Venereol.), Amsterdam, 2 : 67–68, Jan. 1948.]

Une orientation nouvelle en France de la lutte contre les maladies vénériennes. New orientation in France with regard to the control of venereal diseases. H. Gounelle and P. Girault. 55 : 47–48, 1947. [Abstracted in Excerpta Med. (Sec. 13—Dermat. & Venereol.), Amsterdam, 2 : 41–42, Jan. 1948.]

Les accidents d'intolérance à la pénicilline. Manifestations of penicillin intolerance. L. De Gennes, H. Bricaire, C. Laroche and J. Nelhil. 55: 161–162, 1947. [Abstracted in Excerpta Med. (Sec. 13—Dermat. & Venereol.), Amsterdam, 2: 87, Jan. 1948.]

PROC. SOC. EXPER. BIOL. & MED., UTICA

Streptomycin as an essential nutrilite. Geoffrey Rake. 67: 249–253, Feb. 1948.

Results of heterophile antibody agglutination and Kahn tests in patients with viral hepatitis. W. P. Havens, Jr., J. M. Gambescia and Marjorie Knowlton. 67: 437–440, Apr. 1948.

Hemolysis with human complement, human cells, and tannic acid: application to complement fixation test. Lewis Thomas and John L. Peck. 67: 475–478, Apr. 1948.

Effect of chloromycetin on experimental infection with psittacosis and lymphogranuloma venereum viruses. Joseph E. Smadel and Elizabeth B. Jackson. 67: 478–483, Apr. 1948.

Administration of chloromycetin to normal human subjects. Herbert L. Ley, Jr., Joseph E. Smadel and Thomas T. Crocker. 68: 9–12, May 1948.

Fate and distribution of penicillin in the body. I. Circulation of penicillin in the lymph. R. J. Schachter. 68: 29–34, May 1948.

Penicillin in the cerebrospinal fluid following parenteral penicillin. William P. Boger, Richard B. Baker and William W. Wilson. 68: 101–106, May 1948.

Oral administration of bacitracin. Glenn C. Bond, Milton J. VanderBrook, Jean L. Wiley and Mary Ann Nook. 68: 395–400, June 1948.

*Therapeutic activity of bacitracin in rabbit syphilis, and its synergistic action with penicillin. Harry Eagle and Ralph Fleischman. 68: 415–417, June 1948.

Therapeutic activity of bacitracin in rabbit syphilis, and its synergistic action with penicillin. Harry Eagle and Ralph Fleischman. Proc. Soc. Exper. Biol. & Med., 68: 415–417, 1948.

The authors review the literature and report on the therapeutic activity of bacitracin in rabbit syphilis when aqueous solutions were injected intramuscularly once daily for 4 days. Data are also presented which suggest a remarkable synergistic action between penicillin and bacitracin.

Experimental methods, materials, and results are reported in detail.

The studies with bacitracin revealed that an intramuscular dose of 2,300 units per kilogram, repeated once daily for 4 days, cured approximately half the animals tested. As little as 1 mg. per kilogram of penicillin (approximately one-fortieth of the CD_{50} dosage of penicillin alone) and 1,280 units per kilogram of bacitracin (approximately one-seventh of the CD_{50} value) were curative if used in conjunction.

The authors state that the relatively small number of animals so far tested makes the results of qualitative rather than quantitative significance. The incomplete data are reported, however, because of the striking synergism noted in the therapeutic effect of penicillin and bacitracin and its possible significance in relation to the treatment of human syphilis.

PUB. HEALTH, LONDON

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CURRENT NOTES AND REPORTS

To the Field

The editor knows that you are more interested in doing a good job than in telling us about it. And that's the way it should be. There are times, however, when a bit of publicity serves as an inspiration to greater achievement for those actively engaged in the projects and as a guideline to readers who have similar problems.

We know that we are asking a real favor when we say, won't you please "probe" into your various activities and see what you find that might be of interest to other areas? We are especially on the alert for new research and training programs, new methods of case finding, educational experiments, successful cooperative projects, surveys, and control technics, and interesting case reports.

Only with your cooperation can we hope to make "Current Notes and Reports" the kind of clearing house for new ideas and information which will be of maximum value to our readers.

Venereal Disease Clinic Directory

The 1948 directory of clinics for the diagnosis and treatment of venereal diseases is in process for publication early in January. Included in this directory are digests of the premarital and prenatal examination laws of the various States, and a summary of the laboratory services furnished by each.

Limited initial distribution will be made. Single copies may be obtained from the Public Inquiries Section, Division of Public Health Methods, Public Health Service, Washington 25, D. C. Additional copies may be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C.

Interviewer's Aid for Venereal Disease Contact Investigation

Issued by United States Navy

The Bureau of Medicine and Surgery, Medical Department, United States Navy, recently issued a comprehensive aid (NAVMED P–1288) to instruct military personnel in contact interviewing and reeducation of patients with venereal disease. This publication represents part of the Navy's intensified drive to effect close coordination and cooperation with civilian health departments in a concerted effort to prevent the spread of venereal diseases.

About one-half of the 51 pages of this publication are used to instruct the interviewer in the technics of eliciting information from a patient regarding contacts. A short section presents specific information for carrying out the uniform contact reporting system which the Navy has instituted for furnishing information on venereal diseases to epidemiological investigators of State and local health departments; and the last section contains visual aids, such as full page photos and diagrammatic views of each of the venereal diseases showing the causative organism and various stages and effects of the diseases, to be used in re-education of the patient.

Only single copies are available at this time for distribution and these will be sent upon request while the supply lasts.

Revision of Two Handbooks

The American Social Hygiene Association has recently announced new editions of "Digest of Laws and Regulations Relating to the Prevention and Control of Syphilis and Gonorrhea" (Publication No. A422), and "Digest of State and Federal Laws Dealing With Prostitution and Other Sex Offenses" (Publication No. A422a).

Each digest gives citations to the codes, reports, and other sources where the original law may be found. Appendixes summarize Federal legislation, vice repressive laws, and premarital and prenatal examination laws of the various States.

Both publications may be purchased from the American Social Hygiene Association, 1790 Broadway, New York 19, N. Y., at $6 per copy, postpaid. In ordering, it is suggested that the publication numbers be used.

STATISTICS

Cases of Venereal Disease Reported to the Public Health Service by State and Territorial Health Departments, Fiscal Year 1948 (By Disease and Stage)

[Known military cases excluded]

Area	Syphilis						Gonorrhea	Chancroid	Granuloma inguinale	Lympho-granuloma venereum
	Total	Primary and secondary	Early latent	Late and late latent	Congenital	Not stated				
District 1—Total	61. 827	11, 803	16, 542	30, 094	2, 012	1, 376	48, 168	1, 024	244	265
Connecticut	1, 336	235	327	548	53	173	1, 000	18	0	0
Delaware	1, 127	276	337	288	30	196	305	2	3	6
Maine	818	406	114	248	33	17	507	8	0	1
Massachusetts	2, 615	697	383	1, 366	169	0	2, 886	18	2	6
New Hampshire	287	63	41	152	29	2	228	6	0	1
New Jersey	8, 250	1, 362	2. 963	3. 664	204	57	5, 904	47	5	11
New York	32, 823	5, 392	7, 098	19, 043	872	418	27, 047	794	178	216
New York City	26, 726	4, 392	6. 553	14, 905	644	232	23, 742	784	177	214
Pennsylvania	13. 378	3, 175	5, 163	4, 276	563	201	9, 572	127	56	24
Philadelphia [a]	8, 059	1, 488	3, 484	2, 645	164	278	8, 838	51	43	17
Pittsburgh [a]	1, 875	610	483	669	113	0	968	4	5	3
Rhode Island	855	104	98	452	47	154	398	4	0	0
Vermont	338	93	18	57	12	158	321	0	0	0
District 2—Total	41, 907	14, 637	14, 530	10. 505	1, 654	581	61, 594	1, 908	482	619
District of Columbia	3, 916	1, 228	1, 260	1, 267	141	20	12, 518	516	41	110
Maryland	6, 939	2, 093	1, 932	2. 327	243	344	8, 277	156	47	35
Baltimore	5, 029	1, 468	1, 467	1, 838	130	126	6, 480	135	38	24
North Carolina	7, 883	3, 415	3, 045	1, 041	382	0	13, 486	467	100	135
South Carolina	7, 511	2, 789	3, 110	1, 335	277	0	9, 824	288	133	168
Virginia	9. 865	3, 044	3. 643	2, 594	367	217	12, 267	363	152	170
West Virginia	5, 793	2, 068	1, 540	1. 941	244	0	5, 222	118	9	1
District 3—Total	64, 102	15, 086	18, 388	26, 093	2, 418	2, 117	63, 415	915	131	252
Illinois	18, 167	4, 474	5, 429	7. 727	536	1	31, 611	359	52	175
Chicago	11, 689	2, 814	3, 931	4, 620	323	1	25. 200	321	51	164
Indiana	5, 291	1, 688	1, 229	2, 102	271	1	2, 818	32	14	9
Kentucky	6, 104	2. 043	1, 542	1, 928	209	382	7, 153	24	4	6
Michigan	13. 891	2, 629	3, 344	5, 702	492	1, 724	10, 221	325	40	44
Ohio	18, 582	3, 951	6. 313	7, 525	793	0	10, 529	164	21	15
Wisconsin	2, 067	301	531	1, 109	117	9	1, 083	11	0	3
District 4—Total	95, 682	22. 678	29, 297	32. 531	4, 288	6, 888	98. 420	3, 483	1, 261	946
Alabama	22, 432	3, 288	6, 049	7. 662	473	4, 960	7, 217	222	74	68
Arkansas	17, 483	2, 386	4, 246	9, 460	1, 299	92	6, 295	256	52	258
Florida	14, 418	4, 769	5, 095	4, 009	460	85	19, 308	461	412	119
Georgia	12, 152	3, 606	4, 019	3, 852	560	115	16, 287	1, 044	301	141
Louisiana	9, 897	2, 845	2, 903	2, 062	520	1, 567	13. 143	696	200	136
Mississippi	9, 997	3, 065	3, 593	2, 618	721	0	12, 422	394	154	165

District 5—Total	25, 468	5, 964	6, 043	11, 647	840	974	38, 034	645	93	230
Arizona	1, 176	447	319	357	53	0	639	8	1	3
California	19, 558	4, 362	4, 840	9, 058	648	650	1, 329	498	89	217
Nevada	626	181	2	385	14	44	29, 825	3	0	1
Oregon	1, 434	354	218	714	30	118	720	36	1	0
Washington	1, 841	482	487	721	43	108	662	84	1	7
Alaska	212	50	73	45	4	40	1, 670	3	0	0
Hawaii	621	88	104	367	48	14	3, 189	13	1	2
District 6—Total	6, 778	730	3, 410	1, 429	1, 147	62	7, 158	180	9	20
Puerto Rico	6, 604	711	3, 313	1, 391	1, 144	45	7, 037	180	7	20
Virgin Islands	174	19	97	38	3	17	121	0	2	0
District 7—Total	15, 659	4, 011	4, 433	5, 977	621	617	12, 475	158	16	24
Iowa	2, 222	547	656	847	110	62	1, 224	0	0	0
Kansas	2. 335	579	539	1, 102	115	0	1, 900	13	0	5
Minnesota	1, 125	262	191	610	41	21	1, 527	0	0	0
Missouri	7, 684	1, 991	2, 435	2, 745	259	254	6, 255	138	16	19
St. Louis	4, 386	925	1, 599	1, 715	147	0	4, 092	115	16	17
Nebraska	1, 394	271	365	465	43	250	849	7	0	0
North Dakota	402	189	70	91	25	27	248	0	0	0
South Dakota	497	172	177	117	28	3	472	0	0	0
District 8—Total	3, 732	1, 124	916	1, 435	156	101	3, 203	37	3	2
Colorado	1, 663	500	430	666	67	0	1, 951	19	2	2
Idaho	731	180	139	312	30	70	478	14	1	0
Montana	682	253	162	214	33	20	259	2	0	0
Utah	393	109	93	171	20	0	357	0	0	0
Wyoming	263	82	92	72	6	11	158	2	0	0
District 9—Total	30. 597	5, 363	7, 773	6, 102	1, 372	9, 987	39, 064	477	86	158
New Mexico	1, 417	371	440	503	103	0	1, 182	36	0	6
Oklahoma	6. 160	1. 198	1, 764	2, 592	275	331	8, 071	77	7	9
Texas	23, 020	3. 794	5, 569	3, 007	994	9. 656	29. 811	364	79	143
Canal Zone	240	32	67	125	2	14	636	26	0	2
Total continental United States	338, 141	80, 528	97, 745	123, 972	13, 309	22, 587	363, 014	8, 631	2. 315	2, 494
Total United States and Territories	345, 992	81, 428	101, 399	125, 938	14, 510	22, 717	372, 167	8, 853	2, 325	2, 518

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[a] Data from VM-820.

Source: Form 8958-B, USPHS—Venereal Disease Division, Office of Statistics 11/9/48 (ML-MC)mjm.

DOCUMENTS SECTION

The JOURNAL *of* VENEREAL DISEASE INFORMATION

Volume 30 February 1949 Number 2

ORIGINAL ARTICLE

Reports of the North Carolina Syphilis Studies. I. An Evaluation of Case-Finding Measures in Syphilis Control 35

John J. Wright, M. D., M. P. H.
Cecil G. Sheps, M. D., M. P. H.

CURRENT LITERATURE 52

CURRENT NOTES AND REPORTS 64

STATISTICS

Diagnostic Observations for Venereal Disease Completed by State and Territorial Health Departments, Fiscal Year 1948 66

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Public Health Service

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In order to facilitate the handling of manuscripts submitted for publication in the JOURNAL OF VENEREAL DISEASE INFORMATION, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the JOURNAL, and should be presented on separate sheets, rather than within text material.

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Reports of the North Carolina Syphilis Studies

I. An Evaluation of Case-Finding Measures in Syphilis Control

John J. Wright, M. D., M. P. H., and Cecil G. Sheps, M. D., M. P. H.[1]

Introduction

The revolutionary developments of the past decade in the control of syphilis are based upon the dramatic progress which has been made during that time in treatment and in public education. The successive developments in these two fields continue to call for a reevaluation of control methods. For this reason, a careful record and analysis of case-finding activities should be of some value. Such a record was available in the area under study. The purpose of this paper is to report on an analysis of the origin of 2,412 newly discovered cases of syphilis in order to determine the relative effectiveness of various case-finding procedures in syphilis control in a combined rural and urban area served by health departments carrying on an average type of syphilis control program—certainly one which is not out of reach of the average health department.

The development of safe, rapidly effective, and easily applied treatment methods has virtually swept away the case-holding problems in syphilis control. Aside from educational and other measures aimed at reducing promiscuity and promoting prophylaxis, the core of the syphilis control program must, therefore, lie in the effectiveness of its case-finding procedures.

It is well recognized that, in terms of case-finding procedures, newly discovered cases of syphilis fall into three large groups, each of which involves quite different activities on the part of a health department. These are:

1. Epidemiology or contact investigation—administrative and field effort directed at selected individuals.
2. Voluntary application or the patient's initiative—educational efforts directed at groups which may or may not be selected.
3. Serologic dragnet—blood testing of groups which may or may not be selected.

It is axiomatic that venereal disease control programs should give the requisite amount of attention to each of these three case-finding procedures.

What, however, is the requisite amount of emphasis in each of these three approaches? How efficient is each of these methods as a case-finding technic when compared with the other two? What is their proper balance in a syphilis control program?

In seeking answers to questions such as these, one finds surprisingly little agreement in the literature. An editorial in the American Journal of Public Health (*1*) states quite definitely that "Case finding by direct epidemiologic investigation is the most immediately effective and the most continuously applicable method for discovering infectious early syphilis." And yet, Pariser (*2*) in a detailed study of a year's experience of a large city clinic states, "However, in spite of all this, with a program literally built around epidemiology, and with an adequate staff under close supervision, epidemiology remained the least productive, by a large margin, of the three major methods of case finding." He then further shakes one's faith in the epidemiologic approach by concluding, "Even the most vigorous 'from whom to whom' approach to the problem can only be an adjunct to other case-finding methods." This latter conclusion is rather typical of the published studies of this problem (*3*).

Recently there appeared a statistical analysis of the reasons for coming to venereal disease clinics in the period July

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[1] From the School of Public Health, University of North Carolina.

These studies are supported jointly by grants from the International Health Division of the Rockefeller Foundation and the North Carolina State Board of Health.

1946 to December 1947, in scattered areas throughout the United States (*4*). The records of 218,584 cases of venereal disease were analyzed. Of these, 21,533 were previously untreated primary or secondary syphilis. In this group, contact investigation brought in 23.9 percent, whereas 64.2 percent came in on their own initiative.

Thus, it would appear from the literature which analyzes the actual experience of health departments, that the epidemiologic approach, logical as it may seem, is not an effective case-finding measure in syphilis control when compared with the case-finding effectiveness of either education or screening procedures (serologic dragnet). The analysis of our data, however, indicates that contact investigation is of crucial importance as a case-finding measure. It would appear further that the method of analysis of such data which is usually used has tended to obscure rather than to reveal the relevant facts.

Source of Material

The North Carolina Syphilis Study was set up in 1940 as a combined project of the International Health Division of the Rockefeller Foundation and the North Carolina State Board of Health. The study area consists of two contiguous parts—the Orange - Person - Chatham Health District, which is a typical southern rural area, and the Durham City and County Health District, which is a typical southern urban area. The population covered is roughly 160,000 over an area of 1,792 square miles. The study headquarters is in the School of Public Health of the University of North Carolina.

The primary purpose of the study is to measure the effectiveness of the methods of syphilis control being used in the area. Data have, therefore, been continuously gathered to provide a base line of information regarding syphilis in the various population groups in the study area by race, age, sex, and marital and socioeconomic status. Analyses of the data accumulated can provide a reasonably accurate basis for determining trends in syphilis incidence and the effectiveness of various control measures.

The Durham City and County Health Department serves both a highly industrialized city and a rural area. The city is situated within the county area of 299 square miles. Out of a total county population in 1940 (*5*) of 80,244, 60,195 (75 percent) lived in Durham City. Negroes formed 35.6 percent of the total population. In 1945, there were 377 industrial[2] employers in this county (*6*) employing, on the average, 22,881 workers. The most important industry is tobacco, employing an average of 6,733 workers in that year. Next in importance are textile and knitting mills, employing 3,626 workers. There is a predominance of females in Durham County, where they formed 52.5 percent, and in Durham City where they constituted 53.6 percent of the total population in 1940.

The venereal disease program is a specialized one and is carried on in a central clinic which is open daily. In addition to the diagnosis and treatment of all venereal disease cases, the clinic handles the numerous individuals who apply for health certificates or for various other legally required examinations. The clinic physician, who is employed on a full-time basis in the health department, also is called upon to see cases referred because of questionable skin conditions. During the study period, the clinic staff has remained fairly constant in numbers while undergoing a frequent turn-over in personnel. The clinic physician has been assisted by a trained male technician who carried out routine inspections and tests on male patients. The nursing staff has included 3 clinic nurses and, from this study, 1 public health nurse who was directly responsible for interviewing patients and stimulating the follow-up activities. A male follow-up worker has been responsible for visiting contacts and lapsed patients. Under special circumstances, certain cases were referred to the nurses on the general staff for visiting. Except for this selected visiting, the 11 general staff nurses do not participate in the venereal disease program. There is an active venereal disease diagnostic and treatment clinic at Duke Hospital in Durham.

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[2] Industrial employment being defined as systematic or habitual employment, generally in manufacturing or trade and commerce, not including agriculture, domestic service, government service, or professional work. It includes only employment covered by the Employment Security Law.

The Orange-Person-Chatham Health Department provides full-time public health services for the above-named 3 rural counties, which had a total population in 1940 (*5*) of 72,827. For reasons outlined elsewhere, the data for Chatham County were not included in this particular study. The 3 counties are all essentially similar rural counties so far as their major demographic characteristics are concerned. In 1940, Orange County had a population of 23,072 with 31.0 percent Negroes, and Person had a population of 25,029, with 36.4 percent Negroes. The area of each of these 2 counties is virtually the same size. Less than 10 percent of the population of each of those counties was employed in industry in 1945 (*6*). The population of both these counties was evenly divided between the sexes. The venereal disease program is part of the generalized public health program carried on by the Orange-Person-Chatham Health Department. During the study period, the medical staff has included 2 full-time physicians. The number of public health nurses has varied, with 7 being the average for the 3 counties. For approximately 4 years of the study period, a lay follow-up worker was employed to locate and visit certain of the venereal disease contacts and patients. During the entire study period, a public health nurse from this study served as consultant to the venereal disease program of the district health department. Venereal disease clinic service has been available to patients in the area as follows: Orange County, 2 special clinics per week; Person County, 1 special clinic weekly; and Chatham County, 2 polyclinics weekly. Interviewing and contact investigation is carried on by the nurses as a part of their work in a generalized program.

Method of Study

The data presented in this communication include all the new cases of syphilis, regardless of stage, which came to the attention of the health department clinics involved during the years 1943 to 1947, inclusive, for the Durham City and County Health Department, and the years 1941 to 1947, inclusive, for the clinics in the counties of Orange and Person. They fell into three groups:

1. Cases diagnosed for the first time in health department clinics.

2. New cases diagnosed by private physicians and immediately referred to the health department clinic for treatment.

3. New cases diagnosed by private physicians and referred to the health department clinic after not more than 1 month's treatment. This time limit on cases originally diagnosed by private physicians and subsequently referred to the clinic was set arbitrarily at 1 month, because it was believed that the individuals in this group might be expected to remember enough about the circumstances leading to the diagnosis of their disease so that the interviewer could obtain an accurate concept of the circumstances and would, therefore, be able to ascertain what the operative factor was in bringing each individual case to diagnosis at the hands of the private physician.

Data from Chatham County were omitted because of special circumstances which militated against the records relating to the origin of each case being consistently reliable.

It is pointed out that cases of reinfection, relapse, and those who had lapsed treatment and returned for care at a later date were not included in this study, because it was believed that these patients, having had some treatment, had therefore been exposed to a measure of directed venereal disease education. When the patient was under the impression that he had been treated for syphilis at some previous time the case was not included, even in instances where the impression of treatment ("shots in the arm" or "shots in the hip") having been offered by the patient, could not be verified.

Classification of Origin of Cases

Contact investigation.—This classification includes all new cases brought to attention by the use of procedures of various kinds related to the tracing of contacts. The contacts were of the following types:

1. Sexual—marital and extramarital.
2. Family—family contacts were generally investigated only under the following circumstances:

(*a*) All siblings of cases of congenital syphilis.

(*b*) Siblings in the same age group as the patient with acquired syphilis when, in the opinion of the interviewer, the follow-up was either necessary or convenient.

(*c*) Previous children of infected mothers who were born during the period when the mother's syphilis status was not clearly negative.

(*d*) All children receiving intimate care (nursing, bathing, sleeping in the same bed, et cetera) from a mother (or an older sibling) with infectious syphilis.

(*e*) Roomers or boarders under the circumstances described in (*b*) and (*d*).

3. Suspected contacts—persons named as friends of the patient or of a sexual contact whom the patient considered promiscuous, yet who are not specifically named as sexual contacts.

Patient's initiative. — Cases placed in this group were those in which the individual came for an examination on his own initiative or on the initiative of a lay person who either gave advice voluntarily or was asked for advice by the patient. This includes cases in which the patient or a layman who advised him (such as a druggist, employer, parent, or sibling) had sufficient knowledge of venereal disease to appreciate the fact that an examination to rule out syphilis was necessary. Also included are the cases of individuals who are promiscuous and know that under those circumstances it is important for them to have regular examinations. These cases can properly be credited to education, either of the patient or of the layman who advised the patient to seek an examination.

Legal.—This was the group of cases which were diagnosed as a result of the screening procedures for syphilis required by law in North Carolina for the following conditions or occupational groups:

1. Prenatal.
2. Premarital.
3. Health certificates which are issued and which are required for the following groups:

(*a*) Food handlers.

(*b*) Domestic servants.

(*c*) Beauticians and barbers.

These examinations are usually done on an annual basis, at least.

Military.—This group includes the cases which were discovered as a result of the screening procedures of selectees, the preinduction examination, and separatees. Until 1943, the selectees in Orange and Person Counties were examined by draft board physicians. Results of the serologic tests for syphilis were returned to the local health department where diagnosis and treatment were carried out, since infected individuals were automatically rejected. The procedure in Durham during this period was similar, except that the men had a genital inspection and serologic tests for syphilis done at the health department. In 1943, the procedure was changed and all selectees went to a camp for preinduction examination. The results of the serologic tests for syphilis were made known to this study. Since most of those with syphilis were inducted and treated, the final diagnosis was never known to the local health department. Individuals rejected for some reason other than their positive serology were referred to the local health department for the determination of their syphilis status.

At the time of separation from military service, four types of patients were referred to civilian health agencies:

1. Those wtih a definite diagnosis, usually primary or secondary.
2. Those with positive or doubtful serology.

3. Those who had completed treatment for syphilis in the Army and needed serologic follow-up.

4. Those who needed serologic follow-up because of having been treated recently with penicillin for gonorrhea.

Thirteen "new" cases were included in the study from this group.

Special survey.—This included the cases which were discovered as a result of screening procedures, most of which were found by the routine preemployment examinations carried out in some of the large industries in the area under study. This examination includes only a serologic test for syphilis, and in only one industrial plant is the test repeated annually. Those individuals with positive serologic tests are referred to the health department for further study. Cases found by regular examinations required by law in the food industry, such as meatpacking plants, were included in the classification "legal."

Routine.—This group consists of the cases found by professional personnel who were possessed of a high level of suspicion of syphilis in their routine work. It includes all cases which were discovered during a routine examination which was performed for reasons other than the presence of the suspicion of syphilis in the mind of the patient, and also other than preemployment examinations in industry (placed in the group "special survey"). The types of cases included in this group were those which were discovered by private physicians during the course of a routine examination for a condition unrelated to syphilis, or those in which the possibility of syphilis was not recognized by the patient himself. Another type of case included is that of syphilis which is discovered in the clinic in patients who originally come to the clinic for the treatment of gonorrhea. Included also were a small number of cases which were discovered because the public health nurse, during her home visiting, recognized circumstances or lesions which led her to arrange an examination for venereal disease.

Suspects.—These are cases in which syphilis is suspected because of the circumstances surrounding the individual at a particular time, or his habits or reputation. Included in this group are cases such as:

1. Jail inmates and those picked up by the police and brought to the health department for examination because of circumstantial evidence of promiscuous behavior.

2. Individuals whom the public health lay investigator advises to have an examination simply because he knows that they are habitués of places such as "beer joints" where promiscuous individuals are often to be found.

3. Cases which are reported by a third party as being persons in whom syphilis might be suspected, again because of special circumstances indicating promiscuity and, therefore, the strong probability of venereal disease.

In the discussion of the data, the term "serologic dragnet" is used. This refers to the combined effect of three of the classifications listed above: legal, military, and special survey.

Analysis of Data

The data were classified and tabulated according to the following characteristics:

1. Race.
2. Type and stage of syphilis.
3. Sex.
4. Origin of case—by case-finding procedure.
5. Health jurisdiction.

The data were also subjected to statistical analysis with a view to testing their significance.[3] The analysis was performed in a manner such that differences in the total number of cases between health jurisdiction, race, sex, et cetera, were recognized with proper allowances being made for them.

The tables present the data which are discussed. It will be noted that in some instances the percentages do not add up to precisely 100 percent. These differences in summation are due to rounding.

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[3] Grateful acknowledgment is made to the Institute of Statistics, Greater University of North Carolina, for assistance in this phase of the analysis.

Results of Study

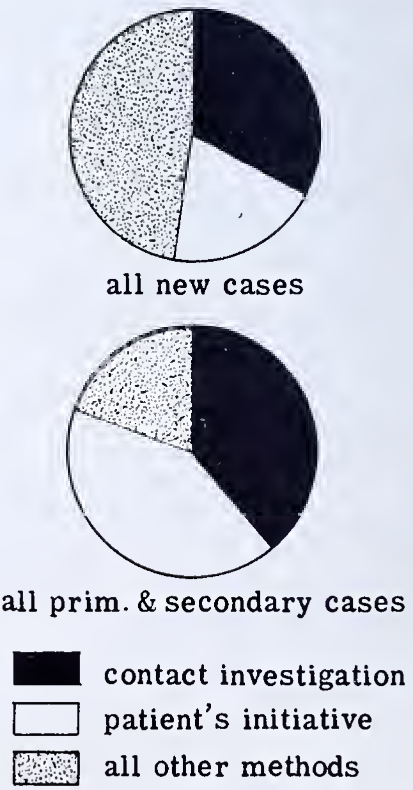
Table 1 presents the data relating to the distribution of cases included in this study in terms of race, sex, and stage and type of syphilis. A total of 2,412 cases was analyzed. Only 178 of these were white cases. Amongst the Negro cases, 54.4 percent were females, closely paralleling the exactly even distribution of the white cases on a sex basis. It will be noted that between 41.5 percent and 50.6 percent of the cases were either primary or secondary for each race-sex group.

Origin of cases by type and stage of syphilis.—Table 2 and figure 1 show the origin of all new cases by type and stage. Out of the total of 2,412 cases, 783 (32.5 percent) were brought to recognition as a result of the contact-tracing procedure. Those cases which can be directly related to education—in other words, those patients who came on their own initiative (as defined above)—provided 488 cases (20.2 percent) of the total group. The cases found by the blood-testing dragnet—that is, the special survey, the legal methods, and the serologic screening in the armed forces—provided 851 (35.3 percent) of the cases. It is to be noted that in the group classified as "routine" there were 186 cases (7.7 percent). From the point of view of controlling the spread of syphilis, one is particularly interested in the cases that are clearly infectious. For this reason, it is interesting to examine the figures for the origin of all primary and secondary cases. The infectious cases comprised 42.8 percent of the entire series under study. Cases classified as early latent were not included in this group of clearly infectious cases, because the criteria usually used in the diagnosis of early latent syphilis are not such that one can be certain of the potential infectiousness of all the cases labeled as "early latent." Thus it is seen that out of the entire group of 1,033 clearly infectious cases (primary and secondary) 394 (38.1 percent) were brought to recognition as a result of the contact-tracing procedure, and 440 cases (42.6 percent) came as a result of the educational process on their own initiative or on that of a lay adviser. It is interesting to note that the number of cases of infectious syphilis found by the serologic dragnet was only 120, forming only 11.6 percent of the entire group of infectious cases.

Special attention is drawn to the shift in relative importance of case-finding procedures when comparison is made between all the cases and the infectious cases. In the infectious group, the patient's initiative (education) and contact investigation increase in importance with a great reduction in the effectiveness of all other methods. This is graphically demonstrated in figure 1. The distribution of case-finding procedures in the noninfectious cases as compared with the infectious-

Figure 1

ORIGIN OF CASES



tious cases was found to be highly significant statistically.

Origin of cases by sex.—Table 3 and figure 2 show the origin of all male cases, both white and Negro. Of the 1,108 cases in this group, 251 patients (22.6 percent) had their origin in the contact-tracing procedure, whereas 332 patients (30 percent) came to diagnosis on their own initiative. The serologic dragnet was responsible for the diagnosis in the case of 418 males, comprising 37.7 percent of the entire group. Of this entire male group, 492 (44.4 percent) were either primary or

Table 1.—***All new cases of syphilis, by race, sex, and type***

Type of syphilis	White				Negro			
	Male		Female		Male		Female	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Primary	19	21.4	8	9.0	229	22.5	82	6.8
Secondary	26	29.2	29	32.6	218	21.4	422	34.7
Total primary and secondary	45	50.6	37	41.6	447	43.9	504	41.5
Congenital	2	2.2	3	3.4	58	5.7	64	5.3
All others	42	47.2	49	55.0	514	50.4	647	53.2
Total	89	100	89	100	1,019	100	1,215	100

Table 2.—***Origin of all new cases of syphilis, by type and stage***

Origin of case	Primary		Secondary		Primary and secondary		Congenital		All others		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Contact investigation	132	39	262	37.7	394	38.1	75	59.0	314	25.1	783	32.5
Patient's initiative	173	51.2	267	38.4	440	42.6	4	3.1	44	3.5	488	20.2
Legal	11	3.2	65	9.4	76	7.4	10	7.9	396	31.6	482	20
Military	9	2.7	20	2.9	29	2.8	5	3.9	230	18.4	264	10.9
Special survey	2	.6	13	1.9	15	1.4	11	8.7	79	6.3	105	4.4
Routine	8	2.4	36	5.2	44	4.2	18	14.2	124	9.9	186	7.7
Suspects	3	.9	22	3.2	25	2.4	1	.8	26	2.1	52	2.2
Unknown	0	0	10	1.4	10	1	3	2.4	39	3.1	52	2.2
Total	338	100	695	100	1,033	100	127	100	1,252	100	2,412	100

Table 3.—***Origin of male cases of syphilis, by type and stage***

Origin of case	Primary		Secondary		Primary and secondary		Congenital		All others		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Contact investigation	67	27	53	21.7	120	24.4	37	61.7	94	16.9	251	22.6
Patient's initiative	159	64.1	144	59	303	61.6	2	3.3	27	4.8	332	30
Legal	3	1.2	10	4.1	13	2.6	4	6.7	85	15.3	102	9.2
Military	9	3.6	20	8.2	29	5.9	4	6.7	229	41.2	262	23.6
Special survey	1	.4	6	2.4	7	1.4	5	8.3	42	7.6	54	4.9
Routine	8	3.2	6	2.4	14	2.8	5	8.3	61	11	80	7.2
Suspects	1	.4	1	.4	2	.4	0	0	3	.5	5	.4
Unknown	0	0	4	1.6	4	.8	3	5.0	15	2.7	22	2
Total	248	100	244	100	492	100	60	100	556	100	1,108	100

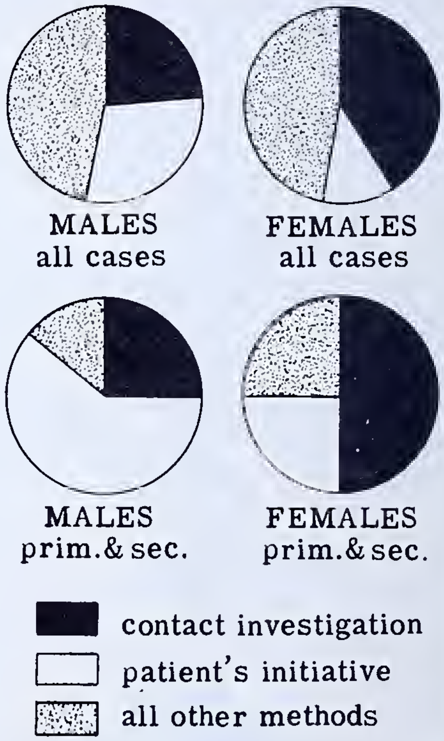
secondary cases. Of these, 120 (24.4 percent) were diagnosed because of the contact-tracing procedure, whereas 303 (61.6 percent) came to attention on their own initiative. The serologic dragnet was responsible for only 49 patients, comprising 10.1 percent of the entire group.

Table 4 and figure 2 show the origin of all female cases, both white and Negro. There were 1,304 cases in this group, including all stages of syphilis. Of this entire group, 532 patients (40.8 percent) were discovered as a result of contact-tracing procedure, whereas only 156 cases (12 percent) came in on their own initiative. It is interesting to note that 433 cases in this group (33.2 percent) were discovered as a result of the serologic dragnet. The analysis showed that 541 female patients were either primary or secondary cases, thus comprising 41.5 percent of the total group. Of these, 274 individuals (50.6 percent) were discovered as a result of contact-tracing procedure, with 137 (25.3 percent) due to the patient's own initiative. Of the entire group, 71 (13.1 percent) were discovered by the serologic dragnet.

Figure 2

ORIGIN OF CASES BY SEX AND TYPE

WHITE and NEGRO



Special attention is called to the difference in the relative effectiveness of the major case-finding measures between males and females. This difference was found to be highly significant statistically. It is demonstrated graphically in figure 2. Among female cases, contact investigation is responsible for finding virtually twice as many cases as it is amongst males, both when all the cases are lumped together regardless of type and also when the clearly infectious cases are considered alone. In the latter group, contact investigation is responsible for fully half the cases found.

Origin of cases by race.—Table 5 shows the origin of all cases among Negro pa-

Table 4.—*Origin of female cases of syphilis, by type, and stage*

Origin of case	Primary		Secondary		Primary and secondary		Congenital		All others		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Contact investigation	65	72.2	209	46.3	274	50.6	38	56.7	220	31.6	532	40.8
Patient's initiative	14	15.6	123	27.3	137	25.3	2	3	17	2.4	156	12
Legal	8	8.9	55	12.2	63	11.6	6	9	311	44.7	380	29.1
Military	0	0	0	0	0	0	1	1.5	1	.1	2	.2
Special survey	1	1.1	7	1.6	8	1.5	6	9	37	5.3	51	3.9
Routine	0	0	30	6.6	30	5.5	13	19.4	63	9	106	8.1
Suspects	2	2.2	21	4.6	23	4.2	1	1.5	23	3.3	47	3.6
Unknown	0	0	6	1.3	6	1.1	0	0	24	3.4	30	2.3
Total	90	100	451	100	541	100	67	100	696	100	1,304	100

tients by sex and type. There were 2,234 patients in this group. Of these, 736 (32.9 percent) were brought to recognition because of the contact-tracing procedure, whereas 446 (20 percent) came in on their own initiative. The serologic dragnet was responsible for 788 patients (35.2 percent). There were 951 infectious cases, comprising 42.6 percent of the total group. Contact tracing was responsible for bringing in 365 patients (38.4 percent). Four hundred patients (42.1 percent) came in on their own initiative, and 111 (11.6 percent) were found by the serologic dragnet.

Table 6 shows the origin of all white cases by sex and type. There were only 178 cases in this group, only 8 percent of

Table 5.—*Origin of Negro cases of syphilis, by type and sex*

Type of syphilis	Contact investigation		Patient's initiative		Legal		Military		Special survey		Routine		Suspects		Unknown		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Primary and secondary	365	38.4	400	42.1	69	7.2	27	2.8	15	1.6	42	4.4	23	2.4	10	1	951	100
Male	114	25.5	270	60.4	12	2.7	27	6.0	7	1.6	12	2.7	1	.2	4	.9	447	100
Female	251	49.8	130	25.8	57	11.3	0	0	8	1.6	30	6	22	4.4	6	1.2	504	100
Congenital	73	59.8	4	3.3	9	7.4	5	4.1	10	8.2	18	14.8	0	0	3	2.4	122	100
Male	36	62.1	2	3.4	3	5.2	4	6.9	5	8.6	5	8.6	0	0	3	5.2	58	100
Female	37	57.8	2	3.1	6	9.4	1	1.6	5	7.8	13	20.3	0	0	0	0	64	100
All others	298	25.7	42	3.6	372	32.0	212	18.3	69	5.9	111	9.6	24	2.1	33	2.8	1,161	100
Male	92	17.9	26	5	78	15.2	211	41.0	40	7.8	54	10.5	3	.6	10	1.9	514	100
Female	206	31.8	16	2.5	294	45.4	1	.2	29	4.5	57	8.8	21	3.2	23	3.6	647	100
All syphilis	736	32.9	446	20	450	20.1	244	10.9	94	4.2	171	7.6	47	2.1	46	2	2,234	100
Male	242	23.7	298	29.2	93	9.1	242	23.7	52	5.1	71	7	4	.4	17	1.7	1,019	100
Female	494	40.6	148	12.2	357	29.4	2	.2	42	3.4	100	8.2	43	3.5	29	2.4	1,215	100

Table 6.—*Origin of white cases of syphilis, by type and sex*

Type of syphilis	Contact investigation		Patient's initiative		Legal		Military		Special survey		Routine		Suspects		Unknown		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Primary and secondary	29	35.4	40	48.8	7	8.5	2	2.4	0	0	2	2.4	2	2.4	0	0	82	100
Male	6	13.3	33	73.3	1	2.2	2	4.4	0	0	2	4.4	1	2.2	0	0	45	100
Female	23	62.2	7	18.9	6	16.2	0	0	0	0	0	0	1	2.7	0	0	37	100
Congenital	2	40	0	0	1	20	0	0	1	20	0	0	1	20	0	0	5	100
Male	1	50	0	0	1	50	0	0	0	0	0	0	0	0	0	0	2	100
Female	1	33	0	0	0	0	0	0	1	33	0	0	1	33	0	0	3	100
All others	16	17.6	2	2.2	24	26.4	18	19.8	10	11	13	14.3	2	2.2	6	6.6	91	100
Male	2	4.8	1	2.4	7	16.7	18	42.8	2	4.8	7	16.7	0	0	5	11.9	42	100
Female	14	28.6	1	2	17	34.7	0	0	8	16.3	6	12.2	2	4.1	1	2	49	100
All syphilis	47	26.4	42	23.6	32	18	20	11.2	11	6.2	15	8.4	5	2.8	6	3.4	178	100
Male	9	10.1	34	38.2	9	10.1	20	22.5	2	2.2	9	10.1	1	1.1	5	5.6	89	100
Female	38	42.7	8	9	23	25.8	0	0	9	10.1	6	6.7	4	4.5	1	1.1	89	100

the number of cases among Negroes. Of these, 47 (26.4 percent) were found through the use of contact-tracing procedures, whereas 42 (23.6 percent) came in on their own initiative. The serologic dragnet brought in 63 cases (35.4 percent). There were 82 infectious cases, comprising 46 percent of the entire group. Contact tracing brought in 29 (35.4 percent) of these. Forty patients (48.8 percent) came in on their own initiative, whereas 9 cases (10.9 percent) were brought in by the serologic dragnet.

It will be noted that the basic difference between the distribution of case-finding procedures in the entire white group as compared with the Negro is the fact that contact investigation is more effective in the Negro group, being responsible for 32.9 percent of all the cases as compared with 26.4 percent in the entire white group. The distribution of the effectiveness of the major case-finding procedures between the two races was found to be highly significant statistically.

Tables 5 and 6 and figures 3 and 4 provide interesting comparative data on a race-sex-specific basis. When the origin of all cases among Negro males is compared with that of all cases among Negro females, it is seen that contact investigation and the patient's initiative together account for virtually the same proportion: 52.9 percent in males and 52.8 percent in females. In the female group, however, contact investigation is of much greater value than in males: females 40.6 percent and males 23.7 percent. When the data for Negro patients with primary or secondary syphilis only are compared on a sex basis, the differences noted above become greatly accentuated. In this in-

Figure 3

ORIGIN OF CASES BY SEX AND TYPE

NEGRO

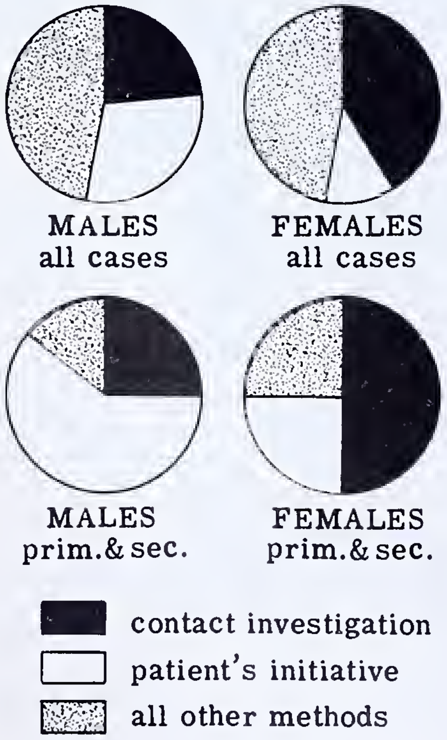
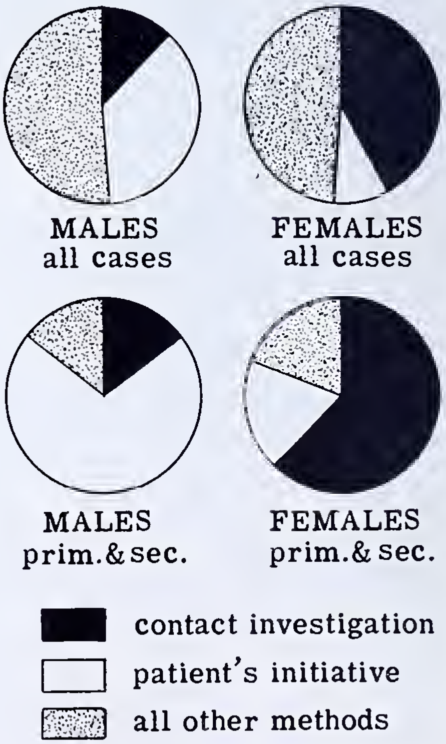


Figure 4

ORIGIN OF CASES BY SEX AND TYPE

WHITE



fectious group, contact investigation and the patient's initiative together are responsible for by far the greatest proportion of the cases; 85.9 percent of males and 75.6 percent of females. The greater relative importance of contact investigation among females referred to above is very striking among the infectious cases: females 49.8 percent and males 25.5 percent.

Sex comparisons among the white cases provide generally the same picture as they do among the Negro patients. When the origin of all cases among white males is compared with that of all cases among white females, it is seen that contact investigation, together with the patient's initiative, account for roughly the same proportion: 48.3 percent in males and 51.7 in females. In the female group it is again seen that contact investigation is of much greater value than in males: females 42.7 percent and males 10.1 percent. When the data for white patients with primary and secondary syphilis only are compared on a sex basis, the differences already noted are again very greatly accentuated. In this infectious group, contact investigation and the patient's initiative together are responsible for by far the greatest proportion of the cases: 86.6 percent of males and 81.1 percent of females. The greater relative importance of contact investigation among females already referred to among the Negroes is even more strikingly demonstrated among the white cases: females 62.2 percent and males 13.3 percent.

Table 7 and figure 5 provide the data for the origin of Negro cases on a sex-specific basis for primary and secondary syphilis separately. It is evident that contact investigation is of crucial importance in the discovery of infectious syphilis among females in both primary and

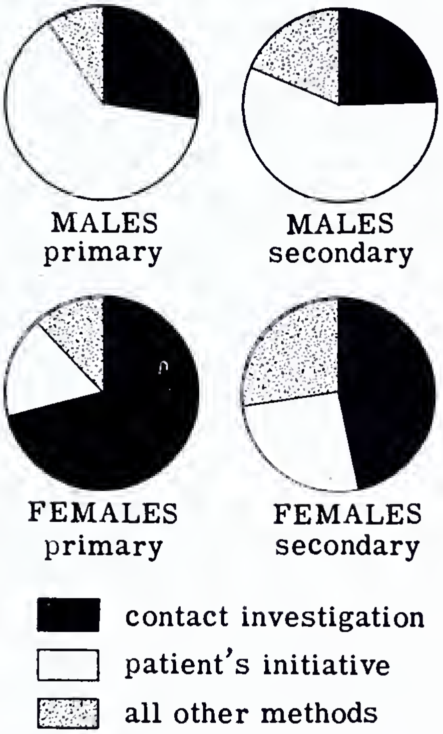


Figure 5

ORIGIN of INFECTIOUS CASES by STAGE and SEX

NEGRO

Table 7.—*Origin of Negro cases of primary and secondary syphilis, by sex*

Origin of case	Primary syphilis				Secondary syphilis			
	Male		Female		Male		Female	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Contact investigation	63	27.5	59	72	51	23.4	192	45.5
Patient's initiative	145	63.3	13	15.8	125	57.3	117	27.7
Legal	3	1.3	7	8.5	9	4.1	50	11.8
Military	8	3.5	0	0	19	8.7	0	0
Special survey	1	.4	1	1.2	6	2.8	7	1.6
Routine	8	3.5	0	0	4	1.8	30	7.1
Suspects	1	.4	2	2.4	0	0	20	4.7
Unknown	0	0	0	0	4	1.8	6	1.4
Total	229	100	82	100	218	100	422	100

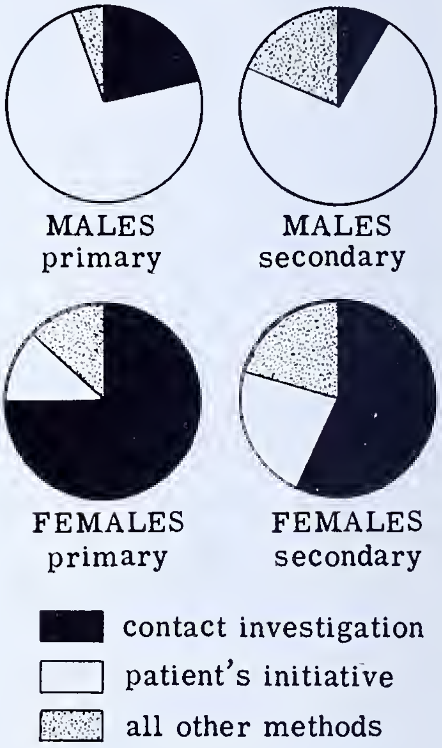
secondary stages. In primary cases the proportions accounted for by the epidemiologic approach were: females 72 percent, males 27.5 percent. In secondary cases the corresponding proportions were: females 45.5 percent, males 23.4 percent. Contact investigation, together with the patient's initiative, were responsible for by far the greatest proportion of the total cases, the proportions for primary cases being: females 87.8 percent, males 90.8 percent. For secondary cases the corresponding proportions were: female 73.2 percent, males 80.7 percent. Though the various legal and routine screening procedures netted a very small proportion of cases, this proportion was somewhat greater among females than males.

Table 8 and figure 6 provide the data for the origin of white cases on a sex-specific basis for primary and secondary syphilis separately. The characteristics of these data are essentially similar to those described above for the Negro cases. One difference which might be worth mentioning is the fact that the proportion of cases discovered due to the patient's initiative was greater in white males than in Negro males in both primary and secondary syphilis. These proportions for primary cases were: white 73.7 percent, Negro 63.3 percent. For secondary cases these proportions were: white 73.1 percent, Negro 57.3 percent.

Figure 6

ORIGIN of INFECTIOUS CASES by STAGE and SEX

WHITE



Origin of cases by health jurisdiction.—Table 9 provides the data for the origin of cases by health jurisdiction. The distribution of case-finding procedures for Durham County, which is essentially an urban area, and Orange and Person Counties, which cover an essentially rural area, are compared. It is seen that for all cases the role of contact investigation is vir-

Table 8.—*Origin of white cases of primary and secondary syphilis, by sex*

Origin of case	Primary syphilis				Secondary syphilis			
	Male		Female		Male		Female	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Contact investigation	4	21.0	6	75.0	2	7.7	17	58.6
Patient's initiative	14	73.7	1	12.5	19	73.1	6	20.7
Legal	0	0	1	12.5	1	3.8	5	17.2
Military	1	5.3	0	0	1	3.8	0	0
Special survey	0	0	0	0	0	0	0	0
Routine	0	0	0	0	2	7.7	0	0
Suspects	0	0	0	0	1	3.8	1	3.4
Unknown	0	0	0	0	0	0	0	0
Total	19	100	8	100	26	100	29	100

Table 9.—*Origin of all cases of syphilis, by health jurisdiction*

Origin of case	Primary and secondary				All other syphilis				Total syphilis			
	Durham County		Orange-Person Counties		Durham County		Orange-Person Counties		Durham County		Orange-Person Counties	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Contact investigation	272	39.0	122	36.3	223	26.6	166	30.7	495	32.2	288	32.9
Patient's initiative	264	37.9	176	52.4	14	1.7	34	6.3	278	18.1	210	24
Legal	61	8.8	15	4.5	262	31.2	144	26.7	323	21.0	159	18.1
Military	17	2.4	12	3.6	118	14.1	117	21.7	135	8.8	129	14.7
Special survey	15	2.2	0	0	83	9.9	7	1.3	98	6.4	7	.8
Routine	35	5.0	9	2.7	71	8.5	71	13.1	106	6.9	80	9.1
Suspects	23	3.3	2	.6	26	3.1	1	.2	49	3.2	3	.3
Unknown	10	1.4	0	0	42	5.0	0	0	52	3.4	0	0
Total	697	100	336	100	839	100	540	100	1,536	100	876	100

tually the same in both jurisdictions, providing as it does 32.2 percent of all syphilis cases in the Durham area and 32.9 percent in Orange and Person. A difference, however, is noted in the relative importance of the patient's initiative, since in Durham 18.1 percent of cases had this origin, while in Orange and Person Counties the comparable proportion was 24 percent. When infectious cases alone are considered, it is again seen that contact investigation brings in virtually the same proportion of cases in the urban area as it does in the rural, viz: Durham 39.0 percent and Orange-Person 36.3 percent. It is noted that there is a difference so far as the relative effectiveness of the patient's initiative and all other methods are concerned. The proportion of cases having their origin in the patient's initiative was: Durham 37.9 percent and Orange-Person 52.4 percent. For all other methods the proportions were: Durham 23.1 percent and Orange-Person 11.3 percent. The difference described above in the distribution of origin of cases as between the two health jurisdictions was found to be statistically significant.

Discussion

The importance of determining the relative effectiveness of various case-finding technics in the syphilis control program is of the first order, especially in these times when radical changes are taking place in treatment procedures—changes which continue to render the treatment of syphilis simpler, more effective, safer, and less expensive than ever before. All this points to a trend, which has already received some attention (7), involving the treatment of an increasing proportion of cases by the private practitioner and a decreasing proportion by health departments. This development is by no means an unmixed blessing so far as organized syphilis control programs are concerned. With the rapid disappearance of treatment and case-holding as problems to be solved, effective education and a positive, organized case-finding program stand out as the touchstones of an effective control program. As private practitioners provide treatment for an increasing proportion of syphilis patients, it becomes much more difficult for a health department to carry out a positive, organized control program, especially so far as contact investigation is concerned. Can education and the various routine serologic screening procedures be relied upon to continue to press forward the war on syphilis?

The literature which might be expected to provide an answer to this question falls into two classes:

1. The studies of experience in terms of the achievements of contact investigation which analyze their data on an absolute basis, using such statistical indices

as contact index, epidemiologic index, brought-to-treatment index, and lesion-to-lesion index, all point to the crucial value of the epidemiologic approach (*8*, *9*, *10*, *11*, *12*).

2. On the other hand, the studies of experience which analyze their data in terms of the relative proportion of total cases of syphilis discovered as a result of contact investigation and other methods uniformly indicate that the epidemiologic approach is the least productive of the major case-finding methods (*2*, *3*, *4*, *13*, *14*, *15*).

Are these latter studies a reflection of the true situation and is the clear logic of the epidemiologic approach, therefore, merely a Utopian dream?

The studies referred to immediately above are usually based on a tabulation of the reason entered under the item on the clinic record, "reason for admission." This item is usually checked by the clinic clerk, who cannot be relied upon to take a consistent interest in this question and who often does not know the real reason for the patient's coming to the clinic. Not uncommonly, the patient deliberately gives a false reason to avoid embarrassment at the front desk. He may have come because of a genital lesion or because he was visited by the follow-up worker as a contact and may say, "I came for a blood test" or "I came for a health card" just to get past the public area of the waiting room in the clinic. This type of inconsistency is often noticed by the clinic physician when he questions the patient more closely. When the clinic physician does obtain the facts, he may or may not place this information on the clinical record. Even if a record is made, it is quite another thing again to have the patient's entire record checked for such inconsistencies and to correct the data given under "reason for admission." Furthermore, the term "reason for admission" is not a clear-cut one and is often interpreted in terms of the referral mechanism and not the "origin of the case," meaning what factor it was that separated that patient from the mass and brought him to recognition (*2*, *3*, *11*, *12*).

It has been possible to eliminate these potent sources of error in this analysis because the syphilis study staff tried to have each patient interviewed by a specially trained nurse. The interview was recorded on a specially designed epidemiological record form which, among other things, aimed at eliciting information leading to an accurate classification so far as actual "reason for admission" is concerned. In the small proportion of cases in which such an epidemiological card had not been completed, the case was placed in the "unknown" column so far as its origin was concerned unless the information in the patient's clinical or other records was unquestionable.

It will be noted that the classification of "origin of case" is a functional one and refers to what brought the patient to recognition, regardless of the referring agency. It is obvious that a series of three or four cases may be referred to the health department clinic, and the case-finding mechanism in each case may be different. Simply to lump these together in terms of the referring agency sheds no light on the functional factors which operated in each instance—the factors which resulted in that case being brought to treatment at the clinic.

The type of analysis reported in this study provides information on the relative role and importance of the primary case-finding technics in an average health department program. It is seen that when the data are broken down and studied on a specific basis by race, sex, and type and stage of syphilis, more light is thrown on the significant aspects of the major case-finding procedures. Only when this is done can the actual vital importance of contact investigation in the *control* of syphilis emerge clearly.

A total of 2,412 new cases of syphilis is analyzed in terms of their origin. Out of this whole group of cases, Negro and white, male and female, 32.5 percent were discovered as a result of contact tracing, 20.2 percent as a result of education (the patient's initiative). The balance of 47.3 percent was discovered by the use of the serologic dragnet and other routine measures. When attention is focused on the infectious cases (primary and secondary), the picture changes radically. The role of contact tracing is enlarged somewhat from 32.5 percent to 38.1 percent. The importance of the patient's initiative is greatly enhanced from 20.2 percent to 42.6 percent. Special attention is drawn to the fact that the role of the serologic dragnet and all measures other than the 2 major ones listed above is drastically minimized in the infectious cases, being reduced from 47.3 percent to 19.3 percent.

Analysis of the data in terms of sex, in addition to type of syphilis, provides additional useful information regarding some specific functions of the major case-finding technics. For all males, contact investigation is responsible for a little less than one-quarter of the cases, and the patient's initiative for a little more than one-quarter; all other methods being responsible for about half the total. Among the infectious male cases, however, it is seen that the proportion of cases which came in on the patient's initiative is more than doubled, rising from 30 percent to 61.6 percent. The role of contact investigation remains about the same, and that of all other methods dwindles to 14 percent of the total. Among all the female cases, it is seen that contact investigation is of much greater importance than among males. When the cases are all lumped together, a little over half are brought in by contact investigation or by the patient's initiative, with the former being responsible for more than three times the latter. In the female infectious group, the role of contact investigation is strengthened from 40.8 percent to 50.6 percent, as is also the patient's initiative from 12 percent to 25.3 percent. The role of all other methods is reduced to one-half of what it is in the entire group of female cases. This enhanced value of contact investigation among females with infectious syphilis is what might be expected simply on the basis of the relative inaccessibility of primary and many secondary lesions among females. Conversely, the easy accessibility of the male genitals to the eye of the patient results in the fact that more male infectious cases will be discovered on the patient's initiative, simply because he can see the lesion and has had sufficient venereal disease education to recognize the possibility of its being due to syphilis. Education of females directed at making them suspicious that a lesion may be due to syphilis would seem to be a procedure of limited usefulness when they are not aware of the presence of the lesion.

The data, when analyzed on the basis of race, showed that contact investigation was responsible for the discovery of a greater proportion of cases among Negroes than among the whites, and the patient's initiative for a smaller proportion. This is probably due to the generally inferior standard of education attained by the Negro population in the study area, thus making them less receptive to venereal disease education and not providing them with an "index of suspicion" as high as that of the white population.

Analysis of the data on a race-sex-specific basis demonstrated that the relative importance of the three major case-finding procedures varied in essentially the same manner between the sexes in the total group, and in infectious cases in both races.

Analysis of the data on a race-sex-specific basis for primary and secondary syphilis separately, shows that they are essentially the same in both races. Consistently, contact investigation is the most important measure in female infectious syphilis, it being responsible for never less than 45.5 percent of cases (Negro-female-secondary) and for as much as 75 percent (white-female-primary). It is pointed out further that in the female infectious group of both races, contact investigation was most effective in the primary cases, being responsible for bringing in 72 percent of all female primaries among Negroes and 75 percent among whites.

When the origin of cases is compared by health jurisdiction, urban and rural, it is seen that contact investigation plays the same relative role in each area. However, a greater proportion of cases came in on the patient's initiative in the rural area and, conversely, a greater proportion of cases came in due to all other methods (those of a routine screening nature) in the urban area. Is education more effective in rural areas? Or is this difference due to the greater effectiveness in urban areas of the routine screening procedures such as legal and special survey? One would tend to feel that the latter is the case, since the occupations and the spatial distribution of the urban population lend themselves to the more effective use of such measures. Further support for this interpretation is provided by the fact that there is an unusually active food-handling sanitation program in Durham, as a result of which this section of the population, in which there is an unusually high incidence of syphilis, is screened for venereal disease not less than and often more than once a year. A further factor probably is the syphilis clinic at Duke Hospital, which attracts some Durham patients who suspect that they may have syphilis. Such patients were not available for interview in the health department and are, therefore, not included in this study. It is noted that the data for the two health jurisdictions were pooled, even though the differences between them were statistically significant. In practical terms, the differences are negligible so far as pooling of the data is concerned when the purpose is to study the effectiveness of the major case-finding methods in an average syphilis control program with special reference to the role of contact investigation.

Conclusions

1. Accurate information on the relative effectiveness of the major case-finding measures is essential for the development of an adequate syphilis control program. Such knowledge can be obtained by a careful analysis of the data relating to the origin of newly discovered cases of syphilis in relation to specific groupings by race, sex, and type and stage of the disease. To obtain such information useful in a program aimed at controlling the *spread* of infection, special attention must be paid to the origin of primary and secondary syphilis on a sex basis.

2. This type of analysis on 2,412 newly discovered cases of syphilis covering a 5-year period in an urban health department and a 7-year period in a contiguous rural health department in the southern United States indicates that:

(*a*) In infectious syphilis, contact investigation was responsible for 38.1 percent of the cases, the patient's initiative for 42.6 percent, and all other methods for only 19.3 percent.

(*b*) In female infectious syphilis, contact investigation is by far the most important case-finding procedure, being responsible for 50.6 percent of all such cases. The importance of this observation is heightened by the fact that in female primary syphilis, contact investigation brought in 72 percent of the Negro and 75 percent of the white cases.

(*c*) In male infectious syphilis, the educational process, as evidenced by the proportion of cases which came in due to the patient's initiative, is the most important case-finding measure, being responsible for 61.6 percent of the cases. Contact investigation was responsible for 24.4 percent.

(*d*) Contact investigation was relatively more effective amongst Negroes than whites.

(*e*) The use of routine serologic screening procedures is the least effective of the three major case-finding procedures in the control of infectious syphilis.

Statistical Appendix

As indicated in the body of the report, the data analyzed covered a period of 7 years in one health jurisdiction and 5 years in the other. The resulting information was then classified into manifold categories as listed under the section entitled "Analysis of Data." Tests of statistical significance between percentages based upon such data assume only binomial variation. This is clearly not the case in these data. Health jurisdiction, sex, race, and other extraneous variations have also influenced the results. Thus, of 2,412 cases analyzed, only 178 were among the white population, 1,304 were among females, and 1,033 were primary and secondary syphilis. Such variations must be taken into account and suitable adjustments made if the resulting comparisons are to be valid.

Analysis of variance technics were used to test the direct effects and interactions of the several factors upon the methods of case finding (*16*). Each of the methods of case finding was expressed as a percentage of the total in groups classified according to sex, race, type of syphilis, year of diagnosis, and health jurisdiction.

A systematic plan of weighting the percentages was adopted (*17*). An angular transformation of the percentages was employed. This tends to stabilize the variance (*18, 19*). A straightforward analysis of variance was then computed upon the transformed data. In this manner, it became possible to study the effect of each factor individually and in combination, adjusted for variations in all remaining factors. This is equivalent to the arithmetic method of standardizing rates for known differences due to sex, race, and other variables.

The tests of significance which were applied consisted of the F-test, or variance-ratio test. They were applied to determine how the factors under consideration, such as race or sex, affected the relative effectiveness of the case-finding procedures. The observed distribution of case-finding procedures was inferred to be fairly consistent from year to year, based upon the significant F-ratio.

Acknowledgement

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CURRENT LITERATURE

Note: Abstracts of any article listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

Am. J. Clin. Path., Baltimore

Kahn reactions with cardiolipin antigen compared with Kahn antigen. II. With a note on a microflocculation procedure with cardiolipin antigen. Reuben L. Kahn and Elizabeth B. McDermott. 18 : 364–374, May 1948.

Plasma concentrations following intramuscular injections of various doses of penicillin. A. Kathrine Miller and William P. Boger. 18 : 421–428, May 1948.

A rapid method for the preparation of serologically active phospholipin and purified lecithin. T. V. Letonoff. 18 : 625–631, Aug. 1948.

An improved antigen for the Kolmer complement-fixation test for syphilis. John A. Kolmer and Elsa R. Lynch. 18 : 731–736, Sept. 1948.

Effect of human cerebrospinal fluid on the dilution bioassay of penicillins G, X and K. Harold A. Tucker. 18 : 737–741, Sept. 1948.

Am. J. Pub. Health, New York

Relative efficiency of the open and the confidential method of reporting causes of death. [VD]. Paul H. Jacobson. 38 : 789–807, June 1948.

Development of a voluntary agency for venereal disease control. Herbert H. Cowper. 38 : 1136–1140, Aug. 1948.

Changing attitude of the Army with regard to venereal diseases. 38 : 1150–1152, Aug. 1948.

Public health in foreign periodicals. George Rosen. 38 : 1156–1160, Aug. 1948.

Am. J. Psychiat., New York

Penicillin therapy in general paresis. George D. Weickhardt. 105 : 63–67, July 1948.

Am. J. Syph., Gonor. & Ven. Dis., St. Louis

* The necessity for treatment of pregnant syphilitic women during every pregnancy. Mary Stewart Goodwin and Mary Streeter Farber. 32 : 409–417, Sept. 1948.

* The rate of development and degree of acquired immunity in experimental syphilis. Harold J. Magnuson and Barbara J. Rosenau. 32 : 418–436, Sept. 1948.

* Experimental gonococcal infection of the rabbit's eye. C. Phillip Miller. 32 : 437–444, Sept. 1948.

* Procaine penicillin G in gonorrhea. An experimental evaluation with observations on blood levels and urinary excretion after small doses. Harold A. Tucker and Mark T. Hockenga. 32 : 445–451, Sept. 1948.

A comparison of the effectiveness of crystalline penicillin with crystalline penicillin plus the enhancement factor in the treatment of gonorrhea. Harold L. Hirsh, Henry Welch, Michael Puzak, S. Ross Taggart, William A. Randall, Clifford V. Price and Velma L. Chandler. 32 : 452–457, Sept. 1948.

Extragenital granuloma inguinale. Report of a case. A. A. Eisenberg. 32 : 458–460, Sept. 1948.

* The evaluation of treatment of paretic neurosyphilis. Ralph W. Grover. 32 : 461–469, Sept. 1948.

* The treatment of neurosyphilis with a combination of malaria and penicillin. Robert R. Kierland, Paul A. O'Leary and Laurence J. Underwood. 32: 470–479, Sept. 1948.

Phenomena of disease in rabbits fed cholesterol and infected with *Treponema pallidum.* A progress report. Chester N. Frazier, Charles D. Boyd, Edgar Grunwaldt, Enid Barker and Margaret Davis. 32: 480–482, Sept. 1948.

* Fever and penicillin therapy in the treatment of congenital syphilitic interstitial keratitis. A preliminary report of nine cases. Irving D. London and Ray O. Noojin. 32: 483–490, Sept. 1948.

Gumma of skeletal muscle: Report of case. Robert R. Kierland and Laurence J. Underwood. 32: 491–493, Sept. 1948.

The necessity for treatment of pregnant syphilitic women during every pregnancy. Mary Stewart Goodwin and Mary Streeter Farber. Am. J. Syph., Gonor. & Ven. Dis., 32: 409–417, 1948.

The authors describe a study begun in 1939 at the Family Syphilis Clinic of the Johns Hopkins Hospital, in which 385 syphilitic mothers, treated before or during a previous pregnancy, have been allowed to go through one or more subsequent pregnancies without additional treatment. The infants of these pregnancies also have been carefully followed to determine the presence or absence of syphilitic infection.

The original criteria for admission to the study included: (1) prior to the deliberately untreated pregnancy, a reasonably accurate history or presumption of maternal infection of at least 2 years' duration, for which 2.0 to 4.0 gm. or more of arsphenamine plus concomitant bismuth or mercury had been received; (2) negative maternal blood serologic tests before and during the current pregnancy; (3) normal maternal spinal fluid tests; (4) no clinical evidence of infection; and (5) at least one previously successful pregnancy, not necessarily after the previous treatment. After an appreciable number of pregnancies without infantile failure had been observed, these criteria were relaxed to include some women whose infections were of less than 2 years' duration at the time of this study, provided that the above treatment had been received prior to this pregnancy; some whose blood serologic tests were still positive despite previous treatment, if no clinical evidence existed; some without spinal fluid examinations; and some with abnormal but inactive spinal fluids.

All patients had quantitative serologic tests and physical examinations at monthly intervals throughout pregnancy during this study, and individuals showing clinical or serologic relapse or reinfection were dropped. All infants were followed with serial serologic and physical examinations, in addition to serial roentgenograms when possible.

Of the 385 patients, 363 had received metal chemotherapy (arsenic and bismuth or mercury), and 22 had been treated with penicillin. In the group of 363 women, who were observed through 570 pregnancies during which maternal treatment was omitted, there occurred 523 live births, 22 stillbirths, and 26 abortions. No evidence of syphilis was found in any of the pathologic examinations made on 8 of the abortions and 12 of the stillbirths, however. The 22 women who were originally treated with 2.4 million units or more of penicillin were observed through 26 subsequently untreated pregnancies; none of the infants has developed congenital syphilis. Of the 549 infants born alive during this study, the approximately 70 percent who have been observed for more than 1 year and the 88 percent who have been carefully followed for more than 2 months are all normal and nonsyphilitic.

The data in this study indicate that it is not necessary to administer antisyphilitic treatment to a syphilitic woman during every pregnancy, provided that she has received either: (1) 4.0 gm. or more of arsphenamine (or the arsenical equivalent), along with concomitant bismuth; or (2) 2.4 million units or more of penicillin, given either in early or late latent syphilis, administered either during a previous pregnancy or during a nonpregnant interval.

It is recommended by the authors that a syphilitic woman be further treated in any pregnancy in which there is clinical evidence of active infection or in which the blood test is positive in a quantitative titer of 16 or more dilution units.

The rate of development and degree of acquired immunity in experimental syphilis. Harold J. Magnuson and Barbara J. Rosenau. Am. J. Syph., Gonor. & Ven. Dis., 32: 418–436, 1948.

This study is the first in a series utilizing a quantitative approach to determine the rate of development and the degree of acquired immunity in experimental syphilis.

By determining the size of inoculum required to produce a given response, a quantitative determination of resistance in animals (rabbits, in this instance) may be made. In this study two variables are concerned: (1) the duration of the original infection prior to treatment versus the degree of acquired immunity; (2) the effect of penicillin versus mapharsen treatment in the development of this immunity.

The original infections were produced by uniform intratesticular or intracutaneous inoculations of the Nichols strain of *Treponema pallidum* and were terminated by treatment with penicillin or mapharsen 3, 6, 12, or 24 weeks after inoculation.

The acquired immunity was challenged 6 weeks after therapy by the inoculation of quantitated numbers of the homologous strain of *T. pallidum* at the site of the original inoculation. Three types of response have been obtained on reinoculation: (1) symptomatic reinfection, in which a darkfield positive lesion developed at the site of reinoculation; (2) asymptomatic reinfection, in which no lesion developed at the site of inoculation, although the animal had been infected as shown by lymph node transfer; (3) immunity, in which no lesion developed and the animal was not infected as shown by lymph node transfer.

As the duration of the immunizing infection increased from 3 to 24 weeks, there was a progressive increase in the number of *T. pallidum* required to produce the symptomatic and asymptomatic responses. At 3 weeks, immunity was small but demonstrable. By the twenty-fourth week, immunity had increased to such a degree that the animals were partially protected (asymptomatic reinfection) against 108 minimal infectious inoculums. Two hundred thousand minimal infectious inoculums were required to produce symptomatic reinfection in 50 percent of these animals and immunity in the remainder.

Immunity that followed either mapharsen or penicillin therapy was essentially the same.

The authors discuss the clinical implications of their findings cognizant of the dangers inherent in transferring animal data to human disease.

Experimental gonococcal infection of the rabbit's eye. C. Phillip Miller. Am. J. Syph., Gonor. & Ven. Dis., 32: 437–444, 1948.

The author describes an experimental gonococcal infection of the rabbit's eye that can be utilized for the testing of new prophylactic agents.

The anterior chamber was selected as the site of inoculation. The rabbits were prepared by an intravenous injection of morphine or demerol and the local application of 5-percent cocaine. The aqueous humor was aspirated and replaced with 0.2 cc. of saline suspension of gonococci.

The gonococci were found to multiply and to invade the intraocular tissues, particularly the lens and ciliary body. In approximately one-third of the inoculated eyes, the infection became chronic and persisted for as long as 14 weeks, the maximum period of observation. The percentage of positive inoculations was roughly proportional to the number of gonococci injected, being 93 percent of eyes infected with approximately 20,000,000 gonococci and falling to 45 percent in eyes injected with approximately 200 gonococci.

Agglutination and complement-fixation tests were run on serums obtained at weekly intervals on all rabbits in which the infection was allowed to become chronic. None developed agglutinins to a significant titer, but a majority developed complement-fixing antibodies, indicating a humoral immune response to a local infection in the eye. The complement-fixation test, however, was no more indicative of existing infection than in man. A positive test merely signified the presence of infection at some time in the past.

Although this experimental infection does not simulate the natural infection in man, it was used to test the effectiveness of gonococcidal agents in vivo. These tests showed that the most effective prophylactic agent was penicillin, which, in a dose as small as 2.5 units, was uniformly effective in sterilizing the anterior chamber of gonococci. Doses of 1 unit sterilized more than 87 percent of the eyes tested. Mild and strong silver protein, even in solutions much stronger than are ever used in man, were ineffective in eliminating gonococci from the anterior chamber, never sterilizing more than 50 percent of the eyes tested. Ointments containing 15 percent sulfathiazole and 30 percent calomel were tested separately and in combination. Sulfathiazole alone or in combination with calomel was 100-percent effective in sterilizing the eyes infected with gonococci when it was made up in an aqueous or vanishing cream base. Thirty percent calomel alone in this vanishing cream ointment was effective in 96 percent of the tests. These ingredients, sulfathiazole and calomel, when made up into an oily or greasy base, succeeded in eliminating gonococci from only 15 to 37 percent of the eyes tested.

Procaine penicillin G in gonorrhea. An experimental evaluation with observations on blood levels and urinary excretion after small doses. Harold A. Tucker and Mark T. Hoekenga. Am. J. Syph., Gonor. & Ven. Dis., 32: 445–451, 1948.

The authors report their observations on the effect of procaine penicillin G in sesame oil on uncomplicated gonorrheal infections.

Fifty patients, white and Negro of both sexes, with acute untreated gonococcal cervicitis or urethritis, were given single intramuscular injections of procaine penicillin G in sesame oil containing either 100, 125, 175, 250, or 500 units per kilogram of body weight. The volumes given ranged from 0.16 to 1.2 cc. Smears and cultures for *Neisseria gonorrhoeae* were done prior to treatment and at intervals of 3, 6, 24, and 48 hours after the single injection. Cure was defined as negative smear and culture, as well as clinical cure at the 48-hour period. Serial blood specimens, obtained by venipuncture ½, 1, 2, 3, 4, and 8 hours after treatment, were assayed for penicillin by the Eagle modification of the Kirby-Rantz method. The total urine excreted by each of four male patients in the lowest dosage categories was collected aseptically at ½-, 1-, 2-, 4-, 8-, 12-, and 24-hour intervals after treatment and similarly assayed for penicillin content.

A study of the serum assays showed that an injection of 18,000 units in the average adult yielded measurable concentrations at 1 and at 2 hours, but not at 3 hours. Serum concentrations were proportioned to the dosages given 1 hour after treatment and subsequently. The percentage cumulative recovery of penicillin in the urine was approximately the same over the 2.5-fold dosage range studied.

It was found that a dosage of 100 units per kilogram failed to cure consistently. The CD_{50} of procaine penicillin G was approximately 175 units per kilogram. Although 250 units per kilogram cured all patients so treated, the authors recommend 0.5 mg. per kilogram as a routine therapeutic dosage in uncomplicated acute gonorrhea. For the average adult this would represent approximately 0.12 cc. of the 300,000 units per cubic centimeter concentration of procaine penicillin G.

The authors state that the intramuscular administration of procaine penicillin G in sesame oil did not cause undue local discomfort, nor were allergic or embolic phenomena encountered.

The evaluation of treatment of paretic neurosyphilis. Ralph W. Grover, Am. J.

Syph., Gonor. & Ven. Dis., 32: 461–469, 1948.

In a review of 1,632 institutional cases of late symptomatic neurosyphilis, the author searches for evidence relating to the criteria of treatment evaluation.

Of the male patients admitted to 2 Veterans Administration neuropsychiatric hospitals over a 26-year period, 1,438 patients (88.1 percent) carried the diagnosis of paresis or taboparesis; 121 (7.4 percent), of meningovascular (cerebrospinal) syphilis; and 73 (4.5 percent), of tabes dorsalis. At the time of study, 366 patients were still in the hospital and constituted 14 percent of the combined hospital populations.

The author selected for study cases having at least two typically paretic (Moore's group III) spinal fluid reports before treatment and clinically suggestive psychosis. Most of these patients had received extensive courses of arsenicals and heavy metals, and many had had malaria as well. In the recent cases, penicillin had dominated therapy.

This series confirms frequent observations that the paretic spinal fluid gradually becomes normal over a period of years after adequate therapy. The author points out the high degree of correlation between decrease of the Wassermann spinal fluid titer and serologic prognosis and suggests that the trend of the Wassermann titer is a more accurate prognostic index than cells and protein in paresis. Also noted is the correlation between the type of clinical picture and the rate of spinal fluid regression. Not a single case was found which showed serologic relapse once definite clinical improvement had been attained.

The author places a limited value on the significance of symptoms in the evaluation of treatment in paresis. Relief of psychosis is significant only when treatment is adequate since symptomatic improvement may be a transient phenomenon if treatment is not adequate. On the other hand, failure of symptoms to respond to treatment does not constitute a treatment failure, or indication for retreatment, when the spinal fluid serologic abnormalities are regressing toward normal.

The author concludes that the basis for comparison of different methods of treatment in paresis should be the ability to produce and maintain serologic negativity, regardless of the rate of regression or change in psychiatric status.

The treatment of neurosyphilis with a combination of malaria and penicillin. Robert R. Kierland, Paul A. O'Leary, and Laurence J. Underwood. Am. J. Syph., Gonor. & Ven. Dis., 32: 470–479, 1948.

In this report, 76 patients with generally severe neurosyphilis who received a combination of malaria and penicillin therapy have been studied.

The following diagnostic categories were employed for the 59 males and 17 females studied: paresis, taboparesis, tabes dorsalis, primary optic atrophy, meningovascular neurosyphilis, and asymptomatic neurosyphilis.

Penicillin was used in varying doses and schemes. The majority (75 percent) of the patients was given a total of 4,000,000 to 6,000,000 units; usually 50,000 to 60,000 units were given intramuscularly every 3 hours for 10 days. Twenty-seven patients were given crystalline penicillin G, the majority receiving 6,000,000 units. Fourteen patients received less than 4,000,000 units of amorphous penicillin. Five patients were given daily injections of penicillin in beeswax and oil; the total dosage varied from 3,600,000 to 6,000,000 units Concurrently, benign tertian malaria was used for all patients. The course of fever consisted of 8 to 10 paroxysms and averaged over 50 total hours of fever over 103° F. The length of observation after treatment ranged from 6 to 44 months.

Spinal fluid examinations that included a Kolmer complement-fixation test, colloidal gold test, total protein test, and cell counts were chosen for evaluating the condition of patients. The spinal fluids were grouped according to the degree of abnormality in the following classification: group III represented the most active and abnormal fluids; group II, the intermediate degree of abnormality; and group I, the least abnormal fluids.

The over-all summary of the spinal fluid examinations reveals that 53 percent of the 76 patients had group III fluids before treatment, while 1 percent were classified similarly when last examined. An "arrested" type of spinal fluid was found in 5 percent of the patients before malaria-penicillin treatment, while 63 percent of the patients had similar findings after treatment. Eighty-eight percent of the patients had minimal (group I) abnormalities, arrested condition, or normal fluids following treatment.

The clinical response was satisfactory in 70 percent of the 63 patients who had symptomatic neurosyphilis before treatment, while 6 percent of the 63 patients were clinically worse following treatment.

A small group of patients receiving crystalline penicillin G combined with malaria did not show a significant difference in improvement, clinically or in the results of the spinal fluid examinations, from those who received amorphous sodium penicillin with malaria.

The authors conclude that a combination of malaria and penicillin is the treatment of choice in severe parenchymatous types of neurosyphilis. With the milder forms of neurosyphilis, such as asymptomatic and meningeal syphilis, patients may first be given the advantage of one or two courses of penicillin alone. If the reactions of the spinal fluid do not become normal or approach normal, and if the clinical findings do not improve, the authors recommend the administration of combined therapy.

Fever and penicillin therapy in the treatment of congenital syphilitic interstitial keratitis. A preliminary report of nine cases. Irving D. London and Ray O. Noojin. Am. J. Syph., Gonor. & Ven. Dis., 32: 483–490, 1948.

This preliminary report concerns nine Negro patients with active syphilitic interstitial keratitis who were treated with combined typhoid fever and penicillin.

Typhoid vaccine was administered daily but given in two doses instead of one to induce fever for the following reasons: (1) ease of administration; (2) the temperature elevations are subject to control and may be discontinued at will; (3) fever therapy may be started immediately upon making the decision to use this form of therapy; (4) elaborate nursing care and equipment are not required; (5) all patients were Negroes, and in the area studied, this race tends to be resistant to a "take" with benign tertian malarial inoculation; (6) satisfactory daily elevations prolonged for 2 to 5 hours may be obtained. The typhoid vaccine used in this study contained one thousand million killed typhoid bacilli per cubic centimeter.

A minimum of 9 and a maximum of 17 daily fever treatments were administered to these 9 patients. The total dosages of penicillin administered varied between 4,000,000 and 6,000,000 units.

Each of the nine patients prior to treatment had poor vision (less than 20/200 in one or both eyes). By the time combined fever and penicillin therapy had been completed all patients had improved vision in the involved eye or eyes. Immediate symptomatic improvement of pain and photophobia and partial clearing of the circumcorneal injection and corneal clouding were noted in all patients within 5 or 6 days after instituting fever therapy.

Six patients were followed for 14 months or longer, and the final visual acuity in the affected eye or eyes varied from 20/60 to 20/100 (without refraction) in five patients. In one patient a relapse occurred in both eyes within 10 months after treatment even though she had had more prolonged and higher temperature elevations than any other member of the group. The fluctuating quantitative Kahn serologic tests did not add helpful data regarding the progress of these patients. In terms of ultimate clinical results, this preliminary study indicates that this regimen is not highly satisfactory.

In conclusion, the author feels that the results of available therapeutic regimens for the treatment of syphilitic interstitial keratitis indicate an urgent need for newer and more effective methods.

ANN. DE DERMAT. ET SYPH., PARIS

General symptoms of Nicholas-Favre disease. P. LeCoulant. 8 : 5–13, Jan. 1948. [Abstracted in Urol. & Cutan. Rev., West Palm Beach, 52 : 309–310, May 1948.]

Recent syphilis, without clinical signs, diagnosed by serology alone. Jules Desneux. 8 : 40, Jan. 1948. [Abstracted in Urol. & Cutan. Rev., West Palm Beach, 52 : 307–308, May 1948.]

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Health agreement between Argentina, Bolivia and Paraguay. 27 : 785–790, Sept. 1948.

Pan American sanitary agreement between Uruguay, Argentina, Brazil and Paraguay. 27 : 791–796, Sept. 1948.

The organization and aims of the Pan American Sanitary Bureau in the Americas and along the United States-Mexico border. M. F. Haralson. 27 : 917–925, Oct. 1948.

BULL. VEN. DIS., BOSTON

Treatment of syphilis with penicillin. Evan W. Thomas. 11 : 1–8, Jan. 1948.

CHINESE M. J., SHANGHAI

Gonorrhea among prostitutes. A survey of the incidence and an attempt at oral sulfadiazine prophylaxis. L. W. Chu and C. H. Huang. 66 : 312–318, June 1948.

CONNECTICUT HEALTH BULL., HARTFORD

A generation of syphilis blood testing. Ruth M. Cowdell. 62 : 236–238, Sept. 1948.

J. A. M. A., CHICAGO

* Newer repository penicillin products. E. W. Thomas, R. H. Lyons, M. J. Romansky, C. R. Rein and D. K. Kitchen. 137 : 1517–1519, Aug. 21, 1948.

* A new vehicle for parenteral repository penicillin therapy. N. Ercoli, W. C. Hueper, L. Landis, B. S. Schwartz and F. J. Queally. 138 : 115–117, Sept. 11, 1948.

* Aureomycin : a new antibiotic with virucidal properties. I. A preliminary report on successful treatment in twenty-five cases of lymphogranuloma venereum. Louis T. Wright, Murray Sanders, Myra A. Logan, Aaron Prigot and Lyndon M. Hill. 138 : 408–412, Oct. 9, 1948.

* Jarisch-Herxheimer reaction in early syphilis. Treated with crystalline penicillin G. Thomas W. Farmer. 138 : 480–485, Oct. 16, 1948.

Newer repository penicillin products. E. W. Thomas, R. H. Lyons, M. J. Romansky, C. R. Rein and D. K. Kitchen. J. A. M. A., 137 : 1517–1519, 1948.

The authors compare, in this study on human subjects, the absorption-delaying properties of a suspension of penicillin salts in peanut oil gelled with aluminum stearates with those of the conventional repository vehicles. The purpose of the study was to observe any untoward effects of repeated injection and to record maintenance of high blood concentrations.

Assays were performed by a modified Rammelkamp method and a cup plate procedure employing Sarcina lutea. Blood levels were determined at regular intervals for the first 24 hours and at 24-hour intervals thereafter. In table form are shown the number of patients, average blood levels, and percentage of patients with blood concentrations of 0.03 unit or higher at successive time intervals following single injections (300,000 units each) of the following repository preparations: (1) sodium penicillin G in peanut oil with 4.8 percent (w/v) white wax; (2) sodium penicillin G in peanut oil with 2 percent (w/v) aluminum monostearate; (3) procaine penicillin G in oil; (4) procaine penicillin G in peanut oil with 2 percent (w/v) aluminum monostearate (large particle); (5) aluminum penicillin in peanut oil with 2 percent (w/v) aluminum monostearate; and (6) procaine penicillin G in peanut oil with 2 percent (w/v) aluminum monostearate (small particle).

Also presented in table form are blood concentrations after prolonged administration of 300,000 units of large particle procaine penicillin per cubic centimeter of peanut oil gelled with 2 percent aluminum monostearate. Sixteen patients received injections once daily for 16 days, and blood levels were determined until the concentration fell below 0.039 unit per cubic centimeter following the last injection. The number of lots of each product tested and the percentage of particles above or below 50 microns in diameter are also tabulated.

The results of this study show that the absorption of all salts of penicillin tested was delayed longer in the aluminum monostearate in peanut oil than when the same salts were suspended in peanut oil alone or in peanut oil plus wax. Further, procaine penicillin in peanut oil gelled with 2 percent aluminum monostearate of small particle size maintained a blood concentration over a much longer period than the same combination with large-sized particle penicillin. No undue irritation or untoward effects were seen in patients receiving the aluminum monostearate in peanut oil gelled products other than the occasional allergic reactions to penicillin, according to the authors.

A new vehicle for parenteral repository penicillin therapy. N. Ercoli, W. C. Hueper, L. Landis, B. S. Schwartz and F. J. Queally. J. A. M. A., 138: 115–117, 1948.

This paper reports a simple and efficient method for maintaining and prolonging an effective plasma level of penicillin. Potassium penicillin was incorporated into a vehicle containing epinephrine suspended in oil, the most efficacious composition being crystalline potassium penicillin, 300,000 units; epinephrine, 0.3 mg.; and vegetable oil, 1 cc.

The preparation was available in ampules containing 1 cc. of oily medium for the 200,000 and 300,000 units of crystalline potassium penicillin doses and 2 cc. for the 400,000- and 600,000-unit doses. After brief shaking of the ampule, the preparation was drawn into a 2- or 5-cc. syringe through a 20- or 21-gage needle and injected into the muscle of the buttocks. Blood for the determination of the penicillin level was removed at varying intervals from the jugular veins of dogs and from the cubital vein of man. The serial dilution method of Rammelkamp was employed for the bioassay of the serum, cultures of *Streptococcus hemolyticus*, type A, group 3, being used as the test organism.

Sixty-six mongrel dogs weighing from 7 to 15 kg. were given intramuscular injections with the penicillin-epinephrine-oil preparation (intracillin) containing 200,000, 300,000 and 400,000 units of penicillin, respectively, and epinephrine in quantities varying from 0.1 to 0.4 mg. per dose. For control purposes, similar amounts of penicillin in isotonic solution suspended in oil and a commercial calcium penicillin-beeswax-oil preparation were administered. The results showed a considerable prolongation of the demonstrable penicillin blood level in all animals which received the penicillin-epinephrine-oil preparation over corresponding doses of penicillin in isotonic sodium chloride solution or penicillin in oil.

The experiments in man were conducted on an ambulatory basis, the general procedure being the same as that used in the dog experiments. Intramuscular administration and subcutaneous administration were employed; the former was effected by injecting the various agents into the buttocks. The blood pressure of the patients was determined directly before the injections were made and at intervals ranging from 30 minutes to 31 hours thereafter. Results of intracillin treatment of 25 patients showed no significant increase of blood pressure which could be attributed to the vasoconstrictor substance injected. A considerable prolongation of the demonstrable blood penicillin level well beyond the 15-hour mark was observed with doses of 300,000, 400,000, and 600,000 units of potassium penicillin, while 200,000 units produced a demonstrable blood penicillin level for more than 12 hours.

Subcutaneous injections of intracillin were administered to 39 patients with gonorrhea, in doses of 150,000, 300,000, and 600,000 units of potassium penicillin. Doses of 600,000 units produced demonstrable blood penicillin levels for 24 hours while doses as low as 150,000 units were effective 15 hours after injection.

The authors conclude from the results of this study that the penicillin-epinephrine-oil preparation produces an effective and demonstrable blood penicillin level after intramuscular injection, and particularly after subcutaneous injection, for 16 to 24 hours when administered with 300,000 units of potassium penicillin. This drug also has the advantage of being easily handled with ordinary syringes and needles.

Jarisch-Herxheimer reaction in early syphilis. Treated with crystalline penicillin G. Thomas W. Farmer. J. A. M. A., 138: 480–485, 1948.

In an attempt to determine the possible prognostic value of the Jarisch-Herxheimer reaction, defined as the transient intensification of the symptoms of early syphilis shortly after the institution of treatment, the author presents a study of this phenomenon based on the results of the treatment of early syphilis, with crystalline penicillin G, at 20 cooperating clinics under the direction of the Syphilis Study Section of the United States Public Health Service.

The incidence of febrile reactions was studied in a group of 939 patients with early syphilis, treated with initial doses of 25,000 to 50,000 units of penicillin G to total doses of 2,400,000 to 4,800,000 units, administered intramuscularly. Of this group, 384 (41 percent) had febrile reactions. No significant race or sex differences in the incidence and severity of febrile reactions were demonstrated. Febrile reactions were observed with equal frequency and severity in 800 patients with seronegative primary, seropositive primary, and secondary syphilis treated with penicillin G.

The Herxheimer reaction in relation to relapse was studied in 395 patients with early syphilis; a febrile reaction was seen in 188 patients (48 percent), of whom 28 (15 percent) had relapsing infections. Among the 207 patients without reactions, relapse occurred in 28 (14 percent). Of the 56 patients with relapses, 28 (50 percent) had febrile reactions with the first course of treatment, and 21 (38 percent) had reactions at the time of re-treatment. Among the patients re-treated, recurrent febrile reactions were no more frequent in those with fever during initial therapy than in those who had no fever.

As to the relationship of reaction to dosage, in patients who were treated with 10 to 120,000 units of penicillin per kilogram of body weight, the incidence of febrile reactions varied from 40 to 56 percent, with no definite trend in relationship to dosage. No febrile reactions were observed when doses of less than 10 units per kilogram of body weight were given.

A study of 49 patients who had shown Herxheimer reactions revealed a uniform temporal pattern of the febrile response to both small and therapeutic doses of penicillin. Observations were made in the same group of patients on the relationship of the reaction to the disappearance of *Treponema pallidum* from darkfield-positive lesions. Herxheimer reactions occurred with single doses of penicillin which were as little as one-tenth the amount required to render syphilitic lesions darkfield negative.

The double Herxheimer reaction was illustrated when the febrile responses of eight patients to small doses of penicillin (10 to 20 units per kilogram of body weight) were repeated on the administration of either a second small dose or a larger therapeutic dose. Results of repeated darkfield examinations remained positive between the first and second doses. However, this reduplication of the reaction was not observed in five patients after repeated large doses of penicillin, results of darkfield examinations in this group becoming negative within 13 hours after administration of the first injection.

The value of the Herxheimer reaction as an aid to the diagnosis of early syphilis is limited by its occurrence in only half the patients treated with penicillin. The mechanism of this reaction in early syphilis is not known, and the author believes that the evidence available does not justify the hypothesis that the reaction is due solely to the sudden destruction of large numbers of spirochetes.

Aureomycin: a new antibiotic with virucidal properties. 1. A preliminary report on successful treatment in twenty-five cases of lymphogranuloma venereum. Louis T. Wright, Murray Sanders, Myra A. Logan, Aaron Prigot and Lyndon M. Hill. J. A. M. A., 138: 408–412, 1948.

This preliminary study of 25 patients

with lymphogranuloma venereum treated with aureomycin represents the first attempt to treat human beings with the new antibiotic.

The patients were divided into three groups: (1) buboes; (2) lymphogranulomatous proctitis, with or without ulceration; and (3) benign cicatricial rectal strictures. Examination of urine, red and white blood cell counts, hemoglobin estimation, Kahn test, Frei test, and urea nitrogen, creatinine, and glucose determinations were made in all cases. The Frei test was positive in all patients. Aureomycin was administered by intramuscular injection in a daily dosage of 10 mg., 20 mg., or 40 mg.

Group I was comprised of eight patients with buboes due to lymphogranuloma venereum; specific lesions had been present from 2 weeks to 2 years. Treatment in this group consisted of one daily intramuscular injection of 20 mg. of aureomycin; two patients received one injection of 20 mg. of aureomycin into the bubo in addition to the regular treatment. All patients showed a reduction in the size of the gland after 4 days of treatment. Three positive Giemsa-stain reactions were obtained from these patients on their admission to the hospital. The smears revealed inclusion and elementary bodies which appeared uniform and took the stain well, but within 48 hours after the start of treatment, specimens from the same buboes showed only occasional elementary and inclusion bodies. Both units appeared pleomorphic and stained poorly. No elementary or inclusion bodies were seen 1 week after treatment.

Group II consisted of three patients with proctitis due to lymphogranuloma venereum who were treated with 20 mg. of aureomycin daily, to total dosages of 80 mg., 200 mg., and 220 mg., respectively. Tenderness and discharge disappeared in two patients after 4 days of treatment, and rectal bleeding stopped in the third patient after 8 days of treatment.

Group III was comprised of 14 patients with benign lymphogranulomatous rectal stricture, the lesions having existed from 2 to 26 years. Following daily injections of 10 mg. or 20 mg. of aureomycin to a total dosage of 160 mg. to 1.0 gm., examination revealed no change in the rectal stricture, but a decided decrease in rectal pain, discharge, and bleeding.

An attempt to determine aureomycin blood levels at varying intervals after injection of the drug revealed no significant levels. However, the authors believe that this may be due to the small amounts of the drug used and to inaccurate methods of assay.

Anemia was noted in some patients within a short time after institution of aureomycin treatment. When a special diluent, in which the antibiotic had been dissolved, was replaced by an isotonic sodium chloride solution, a decrease in the anemic factor was observed. In all instances, even with the use of the special diluent, when a folic acid-iron compound (folvron) was administered simultaneously with the aureomycin, no anemia was noted. There were no apparent toxic effects on any other body system.

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J. SOCIAL HYG., NEW YORK

Premarital and prenatal examination laws in review. Editorial. 34 : 355–357, Nov. 1948.

Progress in State legislation to protect marriage from syphilis. (Maps.) 34 : 358–359, Nov. 1948.

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MEMPHIS M. J., MEMPHIS

Granuloma inguinale treated with streptomycin. Case Report. W. D. Sutliff, R. W. Keeler and Wolcott Dunham. 23 : 210–211, Nov. 1948.

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The choice of sulphonamides. [Gonorrhea] F. Hawking. Revision Corner. 161 : 219–221, Sept. 1948.

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Granuloma inguinale. Report of three cases treated with massive doses of streptomycin. Robert G. Thompson, Claude B. White and Howard Hailey. 41 : 994–997, Nov. 1948.

The treatment of syphilitic interstitial keratitis. Outline of a method of treatment suitable for a rapid treatment center or small hospital. William B. Forsyth. 41 : 1015–1022, Nov. 1948.

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Venereal disease among naval prisoners. Lawrence Z. Freedman. 48: 722–728, Sept.–Oct. 1948.

UROL. & CUTAN. REV., WEST PALM BEACH

The seventh venereal disease? Edward S. Pomeroy. 52: 72–73, Feb. 1948.

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Historical notes on prostitution and venereal disease. 52: 113–116, Feb. 1948.

Military dermatology in general hospitals in the Zone of the Interior and in the Pacific Ocean area in World War II. (Based on observation of 6,683 consecutive cases.) [VD] Tibor Benedek. 52: 160–174, Mar. 1948.

Musings in historical paths and by-paths. [VD] 52: 179–182, Mar. 1948.

Dissecting aneurysm of the aorta: report of case with anuria, and prolongation of life by peritoneal lavage. [Syphilis] Benjamin S. Abeshouse, Louis H. Tankin and Samuel Lerman. 52: 196–203, Apr. 1948.

Reiter's disease. Alfred E. Jones and Ben Seid. 52: 220–222, Apr. 1948.

Urinary tract localizations of poradenolymphitis (Nicolas-Favre disease). [VD] Alfredo Borjas. 52: 227–230, Apr. 1948.

Treatment of gonorrhea with penicillin. From the Tripod. 52: 247–248, Apr. 1948.

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Some remarks on the importance of the reactions of the body in venereal diseases. Jan Roelof Prakken. 52: 406–410, July 1948.

Gonorrhea complicating pregnancy and its relation to ophthalmia neonatorum. J. Bernard Bernstine and George W. Bland. 52: 464–465, Aug. 1948.

Some data on the prevalence and distribution of syphilis in the northern part of the Netherlands. M. Ruiter and H. D. Groen. 52: 465–467, Aug. 1948.

The male bladder. [Syphilis] Dalton K. Rose. 52: 505–509, Sept. 1948.

Case of lymphopathia venereum with coexistent carcinoma of the rectum. Howard U. Kremer. 52: 534–535, Sept. 1948.

Report of a case of probable syphilitic meningitis. Joseph Kanter, Leonard S. Markson and Martin J. Klapman. 52: 676–677, Nov. 1948.

VEN. DIS. BRIEFS, COLUMBUS

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The diagnosis and treatment of neurosyphilis with negative blood and spinal fluid Wassermanns. James Asa Shield. 75: 564–567, Nov. 1948.

WEST. J. SURG., PORTLAND

Uterotubal insufflation with penicillin and streptomycin aerosols. A preliminary report. [Gonorrhea.] Monte Salvin. 56: 500–502, Sept. 1948.

WEST VIRGINIA M. J., CHARLESTON

Ruptured dissecting aneurysm of the ascending aorta with hemopericardium in a twenty-four year old male. Robert U. Drinkard and George L. Armbrecht. 44: 249–252, Sept. 1948.

Announcement

On April 7–8, 1949, there will be held in Washington, D. C., a joint meeting on venereal disease research. On Thursday, April 7, the program will be devoted to a Symposium on Recent Advances in the Study of Venereal Diseases under the auspices of the Syphilis Study Section, National Institutes of Health, Public Health Service, Federal Security Agency.

On Friday, April 8, the second day of the meeting, there will be held the annual scientific session of the American Venereal Disease Association. The business meeting of this Association (limited to members) will be held on the night of April 7, 1949. The time and place of this meeting will be announced later to the membership.

The program for each day will be held in room 1517, Federal Security Building North, beginning at 10 a. m.

All persons interested in this phase of medicine are cordially invited to attend the meeting. Copies of the program will be sent at a later date upon request.

All inquiries should be addressed to: Mr. Francis L. Schmehl, Executive Secretary, Syphilis Study Section, Division of Research Grants and Fellowships, National Institutes of Health, Bethesda 14, Md., or to Dr. William L. Fleming, Secretary, American Venereal Disease Association, 750 Harrison Avenue, Boston, Mass.

Social Hygiene Day

Social Hygiene Day, jointly sponsored by the American Social Hygiene Association and the United States Public Health Service, and observed in February each year throughout the United States, the Territories, and our island possessions, has for its theme in 1949 the protection of family life by wiping out two of the greatest enemies of marriage and parenthood—syphilis and gonorrhea. This year, the Association is holding its annual meeting in Washington, D. C., on February 2, the date chosen for Social Hygiene Day in the District of Columbia.

Special radio programs and newspaper publicity will highlight the events of the day. There will be stimulating discussions of the various aspects of venereal disease problems and outstanding speakers who will analyze past accomplishments and make suggestions for a more complete mobilization of human and scientific resources to bring about even larger gains in the future. In addition, there will be a wide distribution of informational material packaged in attractive kits.

The purpose of Social Hygiene Day is to build citizen understanding of, and active support for, social hygiene objectives. The broad objectives of the Association include the reduction of venereal diseases, repression of prostitution, and, most important of all, the preservation and conservation of wholesome family life. The Association, in carrying out its aims, works in close cooperation with the medical profession; the clergy; health authorities and organizations; pharmacists; leaders in industry, in labor, and in education; welfare organizations; law enforcement agencies; parent-teacher associations; and youth organizations.

Communities which do not have a social hygiene society or committee but which are eager to consider the organization of such a group, or communities which would like to build a program for the observance of Social Hygiene Day in their area, may obtain helpful suggestions and free kits from the Social Hygiene Day Service, The American Social Hygiene Association, 1790 Broadway, New York 19, New York.

Maryland Case-Finding Project Features Free Dance and Movie

Cooperation on the part of tavern owners in Maryland in advertising and sponsoring free dances has made it possible to disseminate venereal disease information to groups of people not ordinarily reached through conventional channels.

This has been demonstrated in the intensified year-long case-finding project along the Eastern Shore which was initiated July 12, 1948, by the Maryland State Health Department, in cooperation with the Public Health Service.

The programs presented at night clubs are built around the movie "Know for Sure," which runs about 22 minutes and has general audience appeal. In addition, the records about venereal disease, "Crossroads Ballad" and "Looking for Lester," are played. The former is a ballad-style folk tale sung in popular rural idiom, and the latter is a tragic tale accompanied by mountain music.

Perhaps the most significant feature of the programs is the informal; open discussion period set aside for the answering of individual questions. A trained speaker is in charge of these discussions and takes this opportunity to emphasize again the importance of discovering syphilis in the early infectious stages. He informs his audience of the facilities and services which are available to them at all times and of the special services which are available during this campaign.

Programs are also presented at churches, schools, clubs, and American Legion posts. They are built around the movie "Know for Sure" but include other material selected from the Columbia University Series of transcribed venereal disease radio programs, and from other sources, to fit the needs of the specific audience for whom it is intended. The program presented in the gymnasium at Princess Anne's College, a coeducational college for Negroes, was especially stimulating because the student body took an active part in the question and answer period. As a result of this meeting, the dean of the college made arrangements with the local county health department for mass blood testing of the entire student body.

Cooperation on the part of the clergy, school officials, 4-H clubs, Elks clubs, American Legion posts, and similar groups in creating interest and providing meeting places has made it possible to reach large audiences. Two rather unusual opportunities for reaching audiences were provided when the local Oyster Workers Union of the Amalgamated Butchers and Meat Packers Union scheduled a meeting for migratory workers in the BPOE Hall in Crisfield, Maryland, and when an invitation came to present the program at a convention of about 200 Negro ministers representing the Eastern Shore of Maryland and Virginia. As a result of the latter meeting, a number of other programs were scheduled.

Examination of Migrant Farm Workers in New Jersey

Serologic tests for syphilis were given this past summer to 3,500 migrant farm workers in Middlesex, Cumberland, and Gloucester Counties in New Jersey. Twelve percent of these (423 persons) showed positive results. This, however, is a considerable drop from the 30-percent positive results reported in the years before penicillin was used. Information elicited from the migrant workers and obtained from records indicated that many of the workers had received penicillin treatment in previous years, either in New Jersey or in the Southern States.

Diagnostic Observations [a] for Venereal Disease Completed by State and Territoria Health Departments, Fiscal Year 1948

Area	Estimated civilian population in thousands	Observations completed [b]	Number completed per 1,000 population	New syphilis cases diagnosed by or admitted to clinics		Observations com pleted per ne syphilis case d agnosed	
				All stages	Primary or secondary	All stages	Primary or secondary
District 1—Total	38, 623	147, 679	3. 8	20, 387	6, 049	7. 2	24.
Connecticut	1, 970	[c] 2, 290	1. 2	458	94	5. 0	24.
Delaware	290	1, 591	5. 5	472	173	3. 4	9.
Maine	884	796	. 9	201	102	4. 0	7.
Massachusetts	4, 623	5, 137	1. 1	869	289	5. 9	17.
New Hampshire	531	70	. 1	8	2	8. 8	35.
New Jersey	4, 582	44, 523	9. 7	3, 213	787	13. 9	56.
New York	14, 140	61, 855	4. 4	8, 228	2, 411	7. 5	25.
New York City	9, 251	53, 484	5. 8	6, 402	1, 709	8. 4	31.
Pennsylvania	10, 498	30, 869	2. 9	6, 781	2, 142	4. 6	14.
Philadelphia	3, 373	20, 942	6. 2	3, 691	1, 058	5. 7	19.
Pittsburgh	2, 100	4, 115	2. 0	1, 172	490	3. 5	8.
Rhode Island	740	548	. 7	157	49	3. 5	11.
Vermont [d]	365	0	----------	0	0	----------	----------
District 2—Total	13, 368	219, 127	16. 4	21, 714	9, 313	10. 1	23.
District of Columbia	831	26, 602	32. 0	1, 979	750	13. 4	35.
Maryland	2, 111	18, 264	8. 7	2, 883	1, 318	6. 3	13.
Baltimore	1, 306	10, 644	8. 2	1, 746	766	6. 1	13.
North Carolina	3, 660	[c] 44, 506	12. 2	6, 768	3, 125	6. 6	14.
South Carolina	1, 929	72, 489	37. 6	5, 310	1, 927	13. 7	37.
Virginia	2, 955	35, 686	12. 1	3. 375	1, 396	10. 6	25.
West Virginia	1, 882	21, 580	11. 5	1, 399	797	15. 4	27.
District 3—Total	31, 930	224, 630	7. 0	16, 421	6, 102	13. 7	36.
Illinois	8, 364	72, 551	8. 7	4, 082	1, 487	17. 8	48.
Chicago	4, 645	64, 973	14. 0	3, 067	1, 007	21. 2	64.
Indiana	3, 833	12, 795	3. 3	1, 338	597	9. 6	21.
Kentucky	2, 761	48, 614	17. 6	3, 016	1, 416	16. 1	34.
Michigan	6, 059	27, 399	4. 5	2, 946	1, 047	9. 3	26.
Ohio	7, 667	59, 868	7. 8	4, 806	1, 473	12. 5	40.
Wisconsin	3, 216	3, 403	1. 0	233	82	14. 6	41.
District 4—Total	17, 841	1, 178, 246	66. 0	64, 042	14, 680	18. 4	80.
Alabama	2, 827	538, 602	190. 5	18, 577	1, 292	29. 0	416.
Arkansas	1, 912	120, 505	63. 0	7, 530	1, 055	16. 0	114.
Florida	2, 280	132, 351	58. 0	7, 109	2, 364	18. 6	56.
Georgia	3, 114	243, 705	78. 3	10, 727	3, 145	22. 7	77.
Louisiana	2, 535	36, 881	14. 5	5, 290	1, 838	7. 0	20.
Mississippi	2, 087	53, 859	25. 8	9, 781	2, 951	5. 5	18.
Tennessee	3, 086	52, 343	17. 0	5, 028	2, 035	10. 4	25.
District 5—Total	14, 742	121, 414	8. 2	7, 631	2, 759	15. 9	44.
Arizona	637	10, 338	16. 2	556	252	18. 6	41.
California	9, 688	73, 948	7. 6	5, 565	1, 932	13. 3	38.
Nevada	139	1, 637	11. 8	119	37	13. 8	44.
Oregon	1, 544	6, 592	4. 3	462	231	14. 3	28.
Washington	2, 319	25, 162	10. 8	801	282	31. 4	89.
Alaska [b]	----------	0	----------	0	0	----------	----------
Hawaii	415	3, 737	9. 0	128	25	29. 2	149.
District 6—Total	2, 065	145, 437	70. 4	7, 916	892	18. 4	163.
Puerto Rico	2, 039	138, 027	67. 7	7, 757	873	17. 8	158.
Virgin Islands	26	7, 410	282. 7	159	19	46. 6	390.
District 7—Total	13, 690	50, 574	3. 7	4, 354	1, 363	11. 6	37.
Iowa	2, 590	1, 633	. 6	300	152	5. 4	10.
Kansas	1, 913	7, 965	4. 2	707	192	11. 3	41.
Minnesota	2, 888	9, 996	3. 5	160	61	62. 5	163.
Missouri	3, 901	23, 122	5. 9	2, 927	861	7. 9	26.
St. Louis	1, 584	14, 279	9. 0	1, 559	328	9. 2	43.
Nebraska	1, 282	6, 144	4. 8	155	48	39. 6	128.
North Dakota	541	75	. 1	10	7	7. 5	10.
South Dakota	575	1, 639	2. 8	95	42	17. 3	39.

See footnotes at end of table.

Diagnostic Observations for Venereal Disease Completed by State and Territorial Health Departments, Fiscal Year 1948—Continued

Area	Estimated civilian population in thousands	Observations completed[a]	Number completed per 1,000 population	New syphilis cases diagnosed by or admitted to clinics		Observations completed per new syphilis case diagnosed	
				All stages	Primary or secondary	All stages	Primary or secondary
District 8—Total	3,037	15,371	5.1	520	206	29.6	74.6
Colorado	1,127	3,313	2.9	218	87	15.2	38.1
Idaho	525	8,542	16.3	92	31	92.8	275.5
Montana	487	601	1.2	34	10	17.7	60.1
Utah	638	2,101	3.3	143	64	14.7	32.8
Wyoming	260	814	3.1	33	14	24.7	58.1
District 9—Total	9,843	225,524	22.9	13,619	3,730	16.6	60.5
New Mexico	538	5,456	10.1	285	64	19.1	85.2
Oklahoma	2,275	80,344	35.3	2,098	750	38.3	107.1
Texas	7,030	139,724	19.9	11,236	2,916	12.4	47.9
Total Continental United States	142,659	2,178,828	15.3	148,560	44,177	14.7	49.3
Total, United States and Territories	145,139	2,328,002	16.0	156,604	45,094	14.9	51.6

[a] For purposes of this report, a diagnostic observation is an examination of a person to determine the presence or absence of venereal disease other than observations to determine response to therapy.

[b] Excluding observations dropped or transferred.

[c] Data incomplete; estimated by applying ratio of reported infected to not infected diagnoses to the total new cases reported.

[d] No public venereal disease clinics.

Source: Bureau of the Census population reports: States—Series P–25, No. 12, July 1947: Cities—Series P–21, Nos. 8, 12, 15, 25, 28, 29, April 1947; Territories—Series P–46, No. 9, July 1945. Observations and diagnosed case data from USPHS–Revised Form 8954-A. USPHS—Division of Venereal Disease, Office of Statistics 11/10/48 (MC–RR)mjm.

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ORIGINAL ARTICLE

Fever-Chemotherapy in Early Syphilis 69

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George X. Schwemlein, *Surgeon (R) (Inactive)*
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Frederick Plotke, M. D., M. P. H.
Erwin E. Peters, M. D.
H. Worley Kendell, M. D.
Arthur A. Rodriquez, M. D.

CURRENT LITERATURE 86

CURRENT NOTES AND REPORTS 91

STATISTICS

Syphilis and Gonorrhea Reported, First Quarter Fiscal Year 1949 . 92

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In order to facilitate the handling of manuscripts submitted for publication in the Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

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Chief, Division of Venereal Disease

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Fever-Chemotherapy in Early Syphilis[1]

Jack Rodriquez, M. D.;[2] George X. Schwemlein, Surgeon (R) (Inactive),[3] Theodore J. Bauer, Medical Director,[4] United States Public Health Service; Frederick Plotke, M. D., M. P. H.,[5] Erwin E. Peters, M. D.,[6] H. Worley Kendell, M. D.,[7] and Arthur A. Rodriquez, M. D.[8]

Introduction

Part I

The introduction of malaria into the treatment of central nervous system syphilis by Wagner-Jauregg (*1*) was a notable achievement. This discovery was adopted and expanded by capable investigators in many lands and eventually provided the stimulus which caused others to search for a less hazardous way of achieving a similar goal. Eventually fever was to be produced by physical methods (*2, 3*) and applied to the treatment of neurosyphilis. The experiences gained during the past decade show that artificial fever therapy is safe, readily tolerated, and has only a minimum of complications, most of which are remediable.

It was a normal sequence of events which developed the proponents of malarial and artificial fever therapy. The brilliant analysis, "The Present Management of Progressive Paralysis," by Wagner-Jauregg, published in 1939 (*4*), is a masterpiece of unprejudiced objectivity. On the basis of his experiences he stated artificial fever therapy of neurosyphilis to be as effective as malarial therapy and that the dangers inherent to both forms of treatment were related to the physical condition of the patient before he was treated.

The report (*5*) of the subcommittee of the Cooperative Clinical Group appointed in 1936 to study and evaluate the various forms of nonspecific therapy used in the treatment of neurosyphilis should end the controversy as to the relative merits of one or the other methods of producing therapeutic fever. Each was found to have its place in modern therapeutics.

However, a wholesome dissatisfaction existed among syphilologists concerning the standard methods of treatment for early syphilis. The majority of syphilitic patients did not receive even sufficient treatment to render them noninfectious because of the long time period required for efficient treatment, the high cost, and the not insignificant number of instances of chemical intoxication (*6*). There were convincing data that insufficient chemical treatment early in the course of syphilis prevents the development of natural specific resistance to the disease (*7, 8*).

The deficiencies in the management of syphilis had been stated with admirable frankness by Moore (*9*): "It must be recognized that even given more clinics, better clinics and free clinics, the control of syphilis by present-day treatment methods is still far from satisfactory. Treatment is too prolonged, too painful, too dangerous, too expensive. Efforts of investigators to develop better and especially shorter methods of treatment should be encouraged."

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[1] From the Chicago Intensive Treatment Center, Venereal Disease Control Program, Chicago Board of Health, in cooperation with the U. S. Public Health Service. Under the direction of Herman N. Bundesen, Senior Surgeon (R) (Inactive), U. S. Public Health Service; President, Chicago Board of Health.

[2] Instructor in Dermatology, University of Illinois College of Medicine; Medical Officer in Charge, Chicago Intensive Treatment Center; Research Associate, Kettering Foundation for Medical Research.

[3] Research Associate, Kettering Foundation for Medical Research; Instructor, Department of Internal Medicine, College of Medicine, University of Cincinnati.

[4] Formerly Venereal Disease Control Officer, Chicago.

[5] Venereal Disease Control Officer, Chicago.

[6] The Monroe Clinic, Monroe, Wis.

[7] Professor of Physical Medicine, University of Illinois.

[8] Assistant Professor of Physical Medicine, University of Illinois.

A rich background of experimental studies of animal and human subjects (*10–13*) provides convincing evidence of the unfavorable influence of high body temperatures on *Spirochaeta pallida*.

Many controlled experiments have shown clinical and immunologic evidence that fever combined with chemotherapy is more effective than either agent employed individually in the treatment of early syphilis in human subjects (*14–18*). Later investigations (*19, 20*) showed that a mode of therapy which combines a subcurative dose of an arsenical with a subcurative session of artificial fever gave superior results in the treatment of experimental syphilis in rabbits when compared with the administration of greater amounts of the drug alone or of fever alone. It had been demonstrated (*21, 22*) that the antispirochetal action (in vitro) of both arsenic and bismuth compounds was increased twofold with a 10° C. rise in temperature range. It had also been observed (*23*) that arsenic and bismuth compounds could be administered with each fever treatment and that fever appeared to exert a protective function against anaphylactic phenomena produced in sensitized individuals by arsenic.

With the development of the continuous, 5-day intravenous-drip method of administering massive doses of arsenicals to patients with early syphilis to achieve the therapia sterilisans magna which Ehrlich originally thought he had found, it was a natural sequel to attempt to combine large doses of arsenicals with fever therapy in attempting to cure primary and secondary syphilis, and to forestall the disastrous late effects.[9]

Early studies (*24*) had shown that fever therapy alone and inadequate amounts of chemotherapy alone over a short period of time were inadequate to control early syphilis in humans. However, the favorable results of the combination of the arsenicals, bismuth, and multiple sessions of artificial fever therapy over a period of several weeks prompted investigations (*25*) in an attempt to compress the treatment into a period of 24 hours.

It was obvious from the onset of these investigations that the massive doses of arsenical employed in the 5-day continuous intravenous method were toxic when employed with artificial-fever therapy. Previous reports (*26–32*) stressed the difficulties in determining the minimum amounts of chemotherapy combined with artificial fever required for the eradication of early syphilis in the human subject. It also offered preliminary data concerning the necessary safeguards required for the treatment of the patient, technical knowledge as regards administering the fever therapy, and the correction of difficulties observed during the administration of the arsenical agents.

It is the purpose of part I of this report to review, after 3 years of observation, the status of patients who were treated with 8 hours of fever, combined with mapharsen and bismuth in 1942 through 1944.

Part II

The advent of penicillin as an effective therapeutic agent for the treatment of early syphilis (*33*) heralded a new era in the control of the disease. It readily became apparent that penicillin had a decided advantage over the older forms of treatment in that it was relatively nontoxic. Although numerous schedules of treatment were outlined, many have been considered inadequate (*34-40*) as regards cumulative failure rates. It was already recognized that schedules requiring injections every 2 or 3 hours were not only expensive as regards hospitalization and time lost from occupation, but were obviously uncomfortable. With the introduction of repository media for penicillin, hospitalization became no longer necessary, but the Out Patient Clinic Section of the Chicago Health Department, employing 10- and 15-day penicillin-oil-beeswax schedules, observed that 13.0 percent and 17.6 percent of the patients, respectively, failed to complete the prescribed course of treatment (*41*).

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[9] According to Simpson et al. (*3*) this investigation had its inception in ideas expressed in a book by Paul De Kruif, Ph. D., entitled "Men Against Death," chap. 9, pp. 267–279, New York, 1932.

With the favorable knowledge gained from the use of artificial fever combined with mapharsen and bismuth in early syphilis (*26*), it was decided to investigate the combination of fever therapy and penicillin in early syphilis. It was first shown (*42*) that penicillin may be safely combined with physically induced fever.

Recent investigations (*40, 43, 44*) show that the addition of multiple fever sessions to 7½-day penicillin schedules of 1.2 and 2.4 million units of aqueous penicillin produced lower cumulative failure rates than the identical amounts of penicillin alone. This fact had previously been suggested by in vitro studies (*45–47*).

As these fever-penicillin schedules were impractical from the standpoint of time alone, i.e., 7½ days of treatment, it was decided to combine the two agents in a shorter interval, i.e., a 30-hour period.

In the initial attempt to shorten the time of treatment to 30 hours a total dose of penicillin consisting of 1.2 million units was combined with 6 hours of fever (*43*). This schedule was abandoned as unsuccessful when 188 patients had been treated with a cumulative failure rate of 37.4 percent at the end of 1 year.

As the then generally accepted "adequate" total amount of penicillin was 2.4 million units over 7½ days, it was decided to increase the amount of penicillin from 1.2 to 2.4 million units with the fever schedule to study the influence of the total dosage factor. In part II of this report, the results of patient's treatment with 6 hours of fever and 2.4 million units of aqueous penicillin in a treatment period of 30 hours (from 1945 through 1946) are presented.

With the assurance that mapharsen and bismuth combined with fever, and penicillin combined with fever, were safe therapeutic procedures, it was logical to assume that the four agents might be safely combined for the treatment of early syphilis in humans.

The synergistic action of mapharsen and penicillin (*45*) had been demonstrated in rabbit syphilis. It had also been shown that the spirocheticidal action of penicillin is enhanced by increase in temperature (*46*).

Part III

Part III of this report deals with the data now available on patients treated in 1946 by the combined use of the four antispirochetal agents—fever, mapharsen, bismuth, and penicillin—in 30 hours, and followed for a period of 12 to 15 months. This schedule produced favorable results which have not been equalled by any other schedule which has been evaluated at this Center for combined primary and secondary syphilis.

I. Six Hundred and Thirty Patients Treated With Fever in Combination With Mapharsen and Bismuth

Method

Although 1,499 patients with early syphilis were treated with fever-chemotherapy, this report is confined to 630 patients who had darkfield-positive lesions of primary and secondary syphilis. This group was treated in the period of November 12, 1942, through May 2, 1944. Forty-one patients did not finish treatment and one died 6 days after treatment, leaving a total of 588 patients.

The patients who completed fever-chemotherapy received various total dosages of mapharsen: 60, 90, 120 mg. and finally a group received 1.76 mg. per kilogram of body weight. The mapharsen was administered by the multiple-syringe method. This was combined with one single dose of 150 mg. of elemental bismuth (2.0 cc. bismuth subsalicylate in oil) administered intramuscularly within 24 hours prior to the day of fever therapy.

In addition to mapharsen and bismuth, each patient also received 8 hours of fever maintained at the level[10] of 106.0° F. rectal in the fever cabinet (Kettering hypertherm).

The total dosage of mapharsen was divided into three equal parts. The first dose was given when the patient's temperature first reached the desired level of 106.0° F., the second dose at the beginning of the third hour of maintained fever, and the third dose at the beginning of the fifth hour of maintained fever. When the 60-mg. dosage was employed, however, this was divided into two equal doses and given as the first two injections in the aforementioned schedule.

No further treatment was given unless clinical or serologic failure occurred, or pregnancy intervened.

The distribution of patients according to age, sex, and race is given in table 1. The age of the patients ranged from 13 to 48 years: 25.0 percent were under 20 years; 41.2 percent were 20 to 24 years of age; and 33.8 percent were 25 years or over. There were 48 (8.2 percent) cases of primary seronegative syphilis (including 1 reinfection); 172 (29.2 percent) cases of primary seropositive syphilis (including 6 reinfections); 331 (56.3 percent) of secondary syphilis (including 4 reinfections); and 37 (6.3 percent) cases of infectious relapsing syphilis (table 2).

Five hundred and eighteen patients had received no previous treatment. Seventy (11.9 percent) patients had been treated as follows: Fifty-two had had long-term chemotherapy of various amounts and duration; nine had fever-chemotherapy of various types; four had the 5-day continuous intravenous mapharsen treatment; four had the modified Schoch-Alexander schedule, and one relapsed after fever-chemotherapy and again after the modified Schoch-Alexander treatment. Eleven of these seventy patients (1.9 percent of the total 588 patients) were considered probable reinfections: seven, after routine long-term therapy; three, after fever-chemotherapy, and one, after the 5-day continuous intravenous method.

Table 1.—***Early syphilis patients treated with fever, mapharsen, and bismuth, by race, sex, and age***

Race and sex	Total	Age in years		
		Under 20	20 to 24	Over 24
Total	588	147	242	199
Male	301	53	113	135
Female	287	94	129	64
White	70	10	16	44
Male	40	3	6	31
Female	30	7	10	13
Other	518	137	226	155
Male	261	50	107	104
Female	257	87	119	51

Table 2.—***Early syphilis patients treated with fever, mapharsen, and bismuth, by therapy schedule and diagnosis***

Therapy schedule (milligrams of mapharsen)	Total	Diagnosis			
		Primary		Secondary	Relapsing
		Seronegative	Seropositive		
Total	588	48	172	331	37
60	128	[1] 12	33	[2] 81	2
90	62	9	[1] 22	27	4
120	18	4	10	4	------
1.76 per kilogram of body weight	380	23	[3] 107	[2] 219	31

[1] Including 1 reinfection.
[2] Including 2 reinfections.
[3] Including 5 reinfections.

Results

The results of treatment at designated intervals are summarized in table 3 for the whole group over a 3-year period.

Figure 1 demonstrates the percentage of successes and failures by diagnosis at the end of 1 and 3 years, respectively.

Figure 2 reveals the percentage of successes and failures by treatment schedules at the end of 1 and 3 years, respectively.

Figure 3 shows the percentages of successes and failures by diagnosis at the end of 1 and 3 years in the group of patients receiving mapharsen on the basis of 1.76 mg. per kilogram of body weight.

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[10] Allows for 0.2° F. (plus or minus) variations from the desired level.

Three hundred and fifty-six of 539 patients with positive pretreatment serologic titers, or 66.0 percent, reversed to negative. The patients with primary syphilis averaged 75.6 percent reversal, secondary syphilis 63.0 percent, and those with relapsing syphilis 48.6 percent. The data on time required to reach seronegativity are biased because of irregularity of follow-up. One hundred and sixty-four patients (46.1 percent), however, were known to be negative within 3 months after treatment, and 273 (76.7 percent) within 6 months. Sixty-nine patients relapsed or were reinfected after becoming negative, representing 43.4 percent of the total 159 failures in the positive group.

One hundred and sixty-seven of the 588 patients were known treatment failures or reinfections at the end of 3 years: 50 of the 128 patients who received 60 mg. of mapharsen; 18 of 62 patients who received 90 mg.; 3 of 18 patients who received 120 mg.; and 96 of 380 patients who received 1.76 mg. of mapharsen per kilogram of body weight (table 3).

The failures are shown by type of failure (including reinfections) and total dosage of mapharsen in table 4.

A lumbar puncture was performed on 554 patients prior to treatment. There were 43 abnormal cerebrospinal fluids in this group. Two hundred and forty-one of the 511 patients with normal pretreatment cerebrospinal fluids had repeat examinations in the posttreatment observation period revealing 21 abnormal fluids. Nineteen of the 43 patients who had abnormal cerebrospinal fluids before treatment were reexamined and 8 showed abnormal fluids while 11 were normal.

One hundred and fifty-eight of the 167 patients who were considered treatment failures or reinfections had pretreatment cerebrospinal fluid examinations, 146 were normal and 12 were abnormal. One hundred of the 146 patients with normal fluids had posttreatment examinations revealing 88 normal and 12 abnormal (12.0 percent neurorecurrence). Ten of the 12 patients with abnormal fluids before treatment were reexamined and showed 6 to be normal and 4 abnormal.

Table 3.—***Early syphilis patients treated with fever, mapharsen, and bismuth, by number of days' observation and treatment results***

Number of days from beginning date of therapy	Number of patients			
	Total observed during period or later	Serologic titer: Seronegative	Serologic titer: Seropositive	Failures during period
0–29	588	53	533	2
30–59	552	113	437	2
60–89	528	187	329	12
90–119	494	233	246	15
120–149	461	253	186	22
150–179	430	255	162	13
180–209	407	260	133	14
210–239	387	268	107	12
240–269	369	267	90	12
270–299	350	266	80	4
300–329	336	261	69	6
330–359	321	253	63	5
360–449	311	258	45	8
450–539	285	239	35	11
540–629	260	224	30	6
630–719	240	214	21	5
720–809	217	191	18	8
810–899	197	179	14	4
900–989	184	172	10	2
990–1,079	163	155	6	2
1,080–1,169	138	132	4	2

Table 4.—***Early syphilis patients treated with fever, mapharsen, and bismuth, by type of failure, and dosage of mapharsen***

Type of failure	Milligrams of mapharsen				
	Total	60	90	120	Per kilogram of body weight
Total	167	50	18	3	96
Clinical	94	28	10	2	54
Serologic	54	17	6	1	30
Reinfections	19	5	2	----	12

Forty-one of 630 patients who began fever-chemotherapy did not complete treatment and were removed from the cabinet for reasons given in table 5. One died 6 days after a complete treatment. The following is a case record of the fatality.

Case 69.—A woman, aged 22, weighing 122 pounds (55 kg.), with a diagnosis of primary syphilis and gonorrheal

Table 5.—***Early syphilis patients treated with fever, mapharsen, and bismuth, by reason for discontinuing treatment***

Reason for discontinuing treatment	Hours of fever		
	Total	7 to 8	Less than 7
Total	41	10	31
Lack of cooperation	21	5	16
Cardiovascular fatigue	6	-----	6
Gastrointestinal disturbances	7	2	5
Dehydration	2	1	1
Hyperpyrexial psychosis	5	2	3

> urethritis and cervicitis, received 8 hours of maintained fever at the 106.0° F. rectal level combined with 150 mg. of elemental bismuth (2.0 cc. bismuth subsalicylate in oil) administered intramuscularly within 24 hours prior to the day of fever-chemotherapy. Mapharsen, 60 mg., in divided doses of 30 mg. each, was administered at the beginning of the first and third hours. Death occurred on the sixth posttreatment day. No postmortem examination was made. The exact cause of death was undetermined, but it was the clinical impression that the cause of death was tuberculous meningitis.

Ten of the 41 patients not completing treatment received from 7 to 8 hours of fever with the prescribed amount of mapharsen and bismuth; the remaining 31 cases received less than 7 hours of maintained fever and varying amounts of mapharsen. These patients were either immediately treated with intensive chemotherapy or placed under observation, depending upon the total amount of treatment administered.

The method of treatment presented was under evaluation in the pre- and early-penicillin era. In fact, many of the 1,499 patients treated were those who could not meet the requirements of the penicillin investigation, and were treated by the method of fever-chemotherapy as it was the most rapid and safest method available in our hands at the time. Further experience in fever-therapy technic was gained as the number of patients in the series increased. Adjustment of the patient's water and electrolyte balance by controlling the fluid intake was eventually accomplished. This reduced the incidence of dehydration or overhydration, and depletion of the electrolyte reserve. There thus resulted a more satisfactory treatment and posttreatment period. Reduction of the cabinet temperatures below that of the patient's temperature was accomplished through the introduction of a modulating control which operates on the humidifying and heating devices of the cabinet. Routine calibration of the rectal thermometers by means of a constant-temperature mercury bath insured the accuracy of the temperature readings. All of these changes materially increased the patient's comfort and reduced the incidence of complications in the patients treated in the latter part of the series.

In part II of this paper, investigations employing penicillin and fever therapy, 6 hours of maintained fever at the 106° F. rectal level were used. It became obvious that the seventh and eighth hours of fever in these original investigations produced many of the causes for discontinuing treatment.

In part III of this investigation, penicillin was added to the method described in this paper, and the amount of fever reduced from 8 to 6 hours. It became evident that such a synergistic therapeutic complex furnishes an effective and short method for the treatment of early syphilis.

Summary

1. Five hundred and eighty-eight patients exhibiting darkfield-positive lesions of early syphilis were given fever, mapharsen, and bismuth.

2. The results of treatment after a 3-year period are presented.

3. The necessary safeguards required for the treatment of the patient, technical knowledge as regards administering the fever therapy, and correction of difficulties observed during the administration of the arsenical agents are outlined.

4. The place of this method of treatment as a basis for syphilotherapeutics is established.

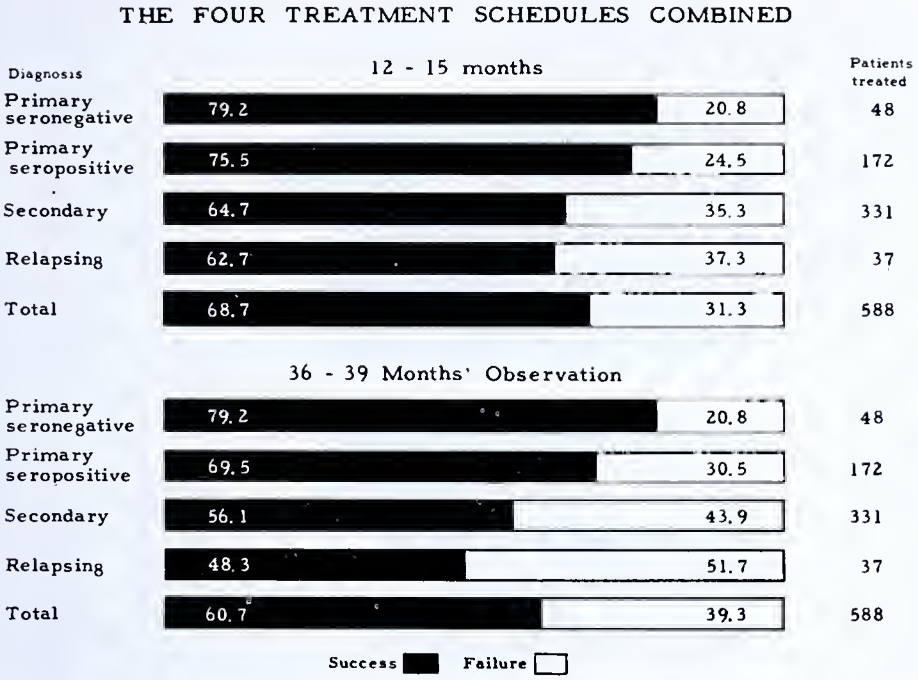

FIGURE 1.—Early syphilis patients treated with fever, mapharsen, and bismuth. Cumulative percentages of successes and failures, 12 to 15 months' and 36 to 39 months' observation. (The four treatment schedules combined.)

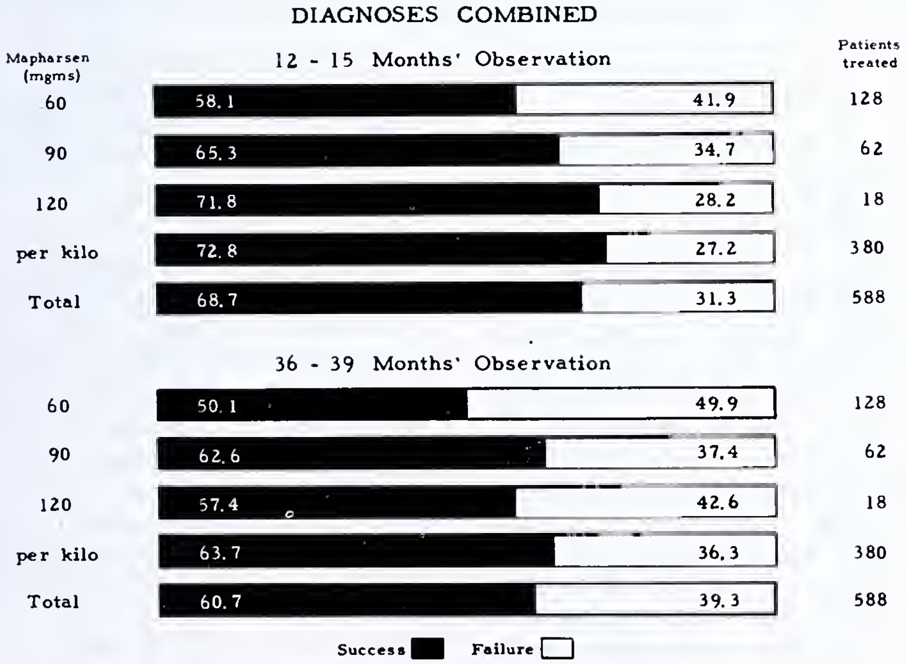

FIGURE 2.—Early syphilis patients treated with fever, mapharsen, and bismuth. Cumulative percentages of successes and failures, 12 to 15 months' and 36 to 39 months' observation. (Diagnoses combined.)

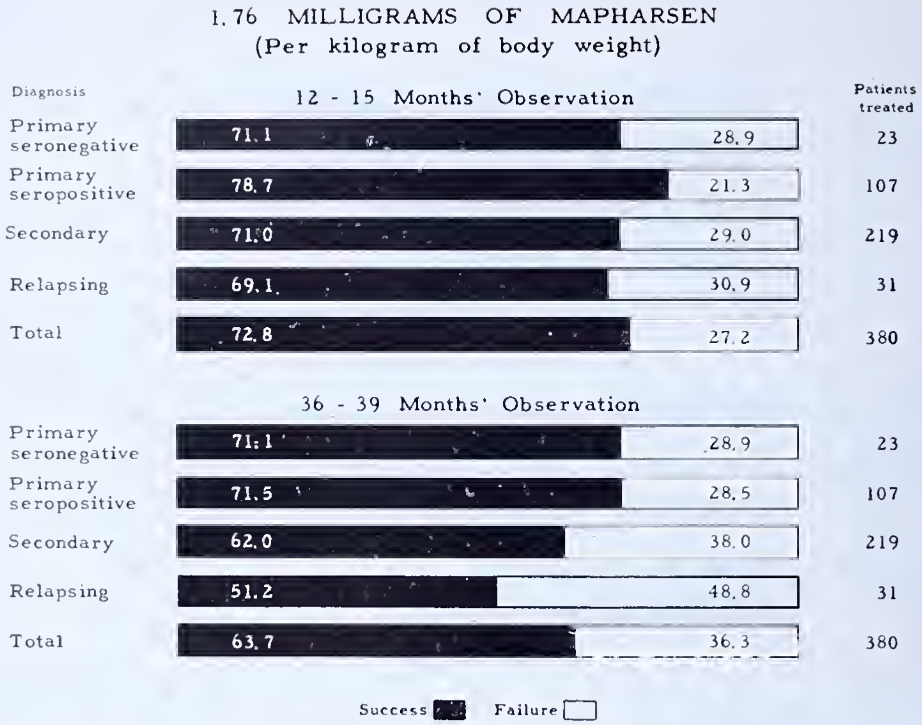

FIGURE 3.—Early syphilis patients treated with fever, mapharsen, and bismuth. Cumulative percentages of successes and failures, 12 to 15 months' and 36 to 39 months' observation. (1.76 mg. of mapharsen per kilogram of body weight.)

II. One Hundred and Thirty-one Patients Treated With Fever in Combination With Penicillin

Method

One hundred and thirty-one patients, exhibiting darkfield-positive lesions of primary or secondary syphilis were considered eligible for treatment. One hundred and thirty patients completed treatment by the following schedule within the period of July 25, 1945, through April 7, 1946. Each patient received 100,000 units of sodium penicillin intramuscularly every 2 hours for 12 doses, beginning at 10:00 a. m. the day prior to fever (total 1,200,000 units). Following the twelfth dose, the patient was placed in the fever cabinet (Kettering hypertherm) and given 6 hours of maintained fever at 106.0° F. rectal level, and at each hour of elevated temperature received 200,000 units of penicillin intramuscularly (1,200,000 units total). This provided a total dose of 2.4 million units of penicillin and 6 hours of fever in approximately 30 hours.

No further treatment was given unless clinical or serologic relapse occurred or pregnancy intervened.

Observation of these patients over a maximum of 27 months and a minimum of 24 months is presented.

The distribution of patients according to age, sex, and race is given in table 6. The age of the patients ranged from 15 to 43 years; 14.6 percent were under 20 years of age; 41.5 percent from 20 to 24 years; and 43.9 percent over 24 years of age. There were 16 (12.3 percent) cases of primary seronegative syphilis; 29 (22.3 percent) of primary seropositive syphilis (including 2 reinfections); 73 (56.2 percent) of secondary syphilis (including 2 reinfections); and 12 (9.2 percent) cases of relapsing early syphilis.

Table 6.—*Early syphilis patients treated with fever and penicillin, by race, sex, and age*

Race and sex	Total	Age in years		
		Under 20	20 to 24	Over 24
Total	130	19	54	57
Male	65	6	22	37
Female	65	13	32	20
White	22	1	7	14
Male	12	1	2	9
Female	10	-------	5	5
Other	108	18	47	43
Male	53	5	20	28
Female	55	13	27	15

Results

The results of treatment at designated intervals are summarized in table 7 for the group as a whole. The results of treatment in the 12 to 15 months' observation period by diagnosis are demonstrated in figure 4 for the 24 to 27 months' observation period.

The time required for healing of lesions was no different than was observed for any of the other treatment schedules.

Table 7.—*Early syphilis patients treated with fever and penicillin, by number of days' observation and treatment results*

Number of days from beginning date of therapy	Number of patients			
	Total observed during period or later	Serologic titer		Failures during period
		Seronegative	Seropositive	
0-29	130	21	109	-------
30-59	119	29	90	-------
60-89	116	40	70	6
90-119	107	50	53	4
120-149	102	55	44	3
150-179	97	56	36	5
180-209	91	61	28	2
210-239	88	61	23	4
240-269	83	63	17	3
270-299	80	63	17	-------
300-329	78	61	15	2
330-359	75	58	14	3
360-449	72	58	12	2
450-539	64	51	9	4
540-629	55	47	5	3
630-719	38	37	-------	1
720-809	21	20	1	-------

Of 114 patients with positive pretreatment serologic titers, 70, or 61.4 percent, reversed to seronegativity, including 21 with primary syphilis, 40 with secondary syphilis, and 9 with relapsing syphilis. Twenty-nine, or 41.4 percent, were known to have become seronegative within 3 months; 51, or 72.9 percent, within 6 months; and 62, or 88.6 percent, within 9 months. The median number of days required to reach seronegativity was 110 for the group of 70. Twelve of the 70 patients reversing to seronegativity, 17.1 percent, were later re-treated: 7 for clinical relapse; 3 for serologic relapse; 1 as a reinfection; and 1 for asymptomatic neurosyphilis.

Forty-two of the total 130 patients were known treatment failures at the end of the 24 to 27 months' observation period. These consisted of 3 cases of relapsing primary syphilis, 13 relapsing secondary syphilis, 23 serologic relapses, and 2 neurorecurrences. One possible reinfection was grouped with the failures.

A lumbar puncture was performed for all but 10 of the patients prior to treatment. There were 12 (10 percent) abnormal cerebrospinal fluids. Of these 12 patients, 7 had repeat examinations from 6 to 17 months later. Four revealed normal and 3 abnormal fluids.

Among the 42 treatment failures, 5 had abnormal spinal fluids before treatment. Of the 5 patients, 2 showed normal posttreatment fluids and 2 abnormal posttreatment fluids; 1 patient was not reexamined. Of the 34 patients with normal pretreatment spinal fluids, who later relapsed, 27 were reexamined: 23 were normal; and 4, or 14.8 percent, abnormal at the time of failure.

Reactions during treatment were of the local and systemic Herxheimer type, which were apparent before fever was induced. One patient did not receive the prescribed amount of treatment because of hyperpyrexial psychosis during fever and is not included in the evaluation. There were no serious reactions in the entire group.

The incidence of gastrointestinal disturbances and dehydration was much lower when the fever therapy was combined with penicillin than when it was combined with mapharsen and bismuth.

Increasing the total amount of penicillin given with fever-therapy produced no added discomfort to the patient. Technically the administration of penicillin and fever was as simple as the administration of fever alone. No investigation was performed using 2.4 million units of penicillin alone in 30 hours as it was already evident that dosages of 10 and 25 million units by the continuous intravenous route were inadequate (*39*). An over-all cumulative failure rate, regardless of stage of disease, was 36.1 percent at the end of the 12 to 15 months' observation period and 43.5 percent at the end of 24 to 27 months' observation period for the 30-hour schedule using 2.4 million units of penicillin and fever. Obviously this schedule of treatment was inadequate. There was little difference when compared to the fever-penicillin schedule using 1.2 million units, which produced a cumulative failure rate of 37.4 percent at the end of 12 to 15 months' observation period.

In figure 5 are shown the cumulative failure rates in the 12 to 15 months' observation period of the groups of darkfield-positive secondary syphilis patients receiving penicillin and those receiving penicillin and fever-therapy in various schedules.

Summary

1. One hundred and thirty patients with darkfield-positive lesions of early syphilis were given 2.4 million units of penicillin over a period of approximately 30 hours, and a single 6-hour session of fever.

2. Attempts to shorten fever-penicillin schedules to the 30-hour schedule were unsuccessful in that the over-all cumulative failure rate was 36.1 percent at the end of 12 to 15 months and 43.5 percent at the end of the 24 to 27 months' observation period.

3. The described schedule of treatment for early syphilis is the basis of a subsequent successful investigation reported in part III.

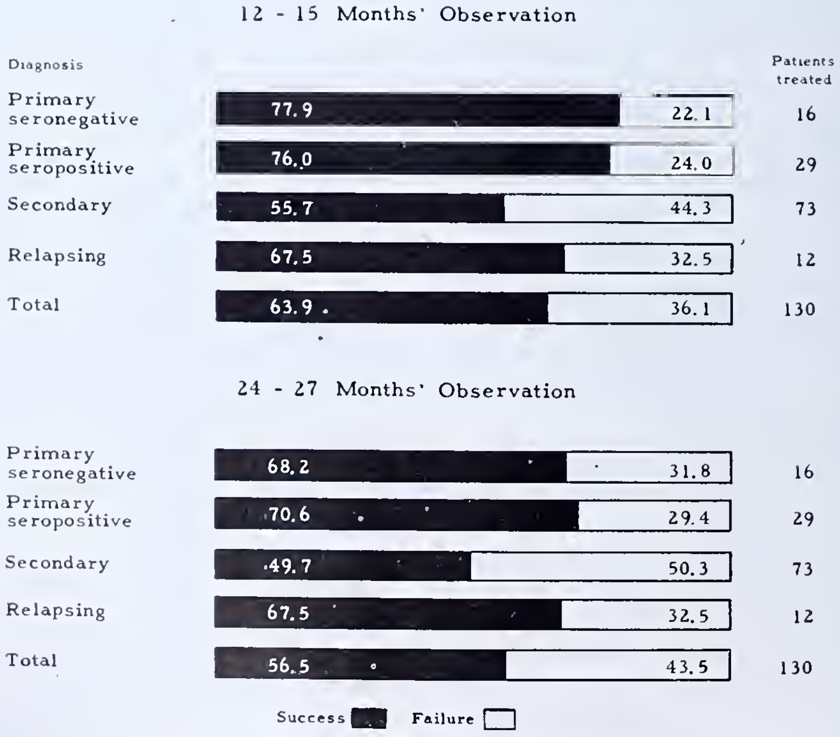

FIGURE 4.—Early syphilis patients treated with fever and pencillin. Cumulative percentages of successes and failures, 12 to 15 months' and 24 to 27 months' observation.

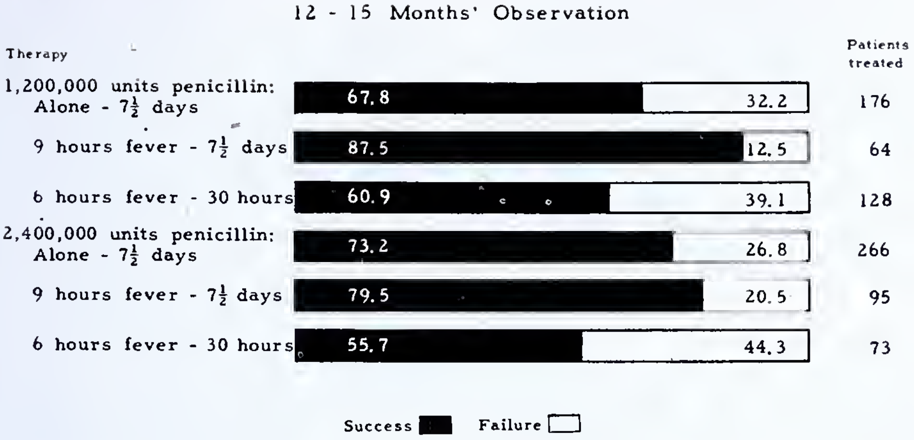

FIGURE 5.—Secondary syphilis darkfield-positive patients treated with penicillin alone and in combination with fever. Cumulative percentages of successes and failures, 12 to 15 months' observation.

III. One Hundred and Forty-one Patients Treated With Fever in Combination With Mapharsen, Bismuth, and Penicillin

Method

A total of 141 patients who had darkfield-positive lesions of primary and secondary syphilis were treated on this schedule. Four cases, 2.8 percent,[11] did not complete the treatment schedule, leaving a total of 137 patients upon which this report is based.

Table 8 gives the distribution of patients by race, sex, and age. There were 23 cases (16.8 percent) of seronegative primary syphilis, 42 (30.6 percent) of seropositive primary syphilis, 66 (48.2 percent) of secondary syphilis and 6 (4.4 percent) cases of relapsing [12] syphilis. One hundred and twenty-two patients were previously untreated for syphilis. In addition to the 6 cases of relapsing syphilis, 8 were diagnosed as reinfections and 1 had minimal treatment prior to admission. The patients all received a thorough diagnostic medical survey, the usual pre- and post-fever management (*30*), and routine follow-up procedures (*26*). The first patient was treated August 1, 1946, and the last November 17, 1946.

The following routine was administered to each of the 137 patients. Six hours of fever at 106.0° F. rectal level were given in the air-conditioned cabinet (Kettering hypertherm). A total of 2.4 million units of sodium salt of crystalline penicillin G was administered intramuscularly. One-half of this total dose was given in a 22-hour period before fever (12 injections of 100,000 units every 2 hours). The second half of the total dose was administered during the maintenance fever (200,000 units at the end of the induction period and repeated hourly for a total of 6 doses). Mapharsen, 1.76 mg. per kilogram of body weight, was injected intra-

Table 8.—***Early syphilis patients treated with fever, mapharsen, bismuth, and penicillin, by race, sex, and age***

Race and sex	Total	Age in years		
		Under 20	20 to 24	Over 24
Total	137	13	67	57
Male	81	3	34	44
Female	56	10	33	13
White	25	2	11	12
Male	16	------	7	9
Female	9	2	4	3
Other	112	11	56	45
Male	65	3	27	35
Female	47	8	29	10

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[11] These four patients completed treatment on other intensive schedules.

[12] Including two cases of relapsing primary and four cases of relapsing secondary syphilis.

venously in three equally divided doses given at the beginning of the first, third, and fifth hours of maintained fever. One hundred and fifty milligrams of elemental bismuth (2 cc. bismuth subsalicylate in oil) were administered intramuscularly approximately 18 hours before the fever session. No further treatment was given unless clinical or serologic failure occurred.

Results

Table 9 shows the number of patients observed, grouped by treatment results and number of days from beginning of therapy.

Table 9.—*Early syphilis patients treated with fever, mapharsen, bismuth, and penicillin, by number of days' observation and treatment results*

	Number of patients			
Number of days from beginning date of therapy	Total observed during period or later	Serologic titer		Failures during period
		Seronegative	Seropositive	
0–29	137	24	113	--------
30–58	129	46	83	--------
60–89	127	60	67	--------
90–119	126	76	47	3
120–149	121	84	37	--------
150–179	120	91	26	3
180–209	113	91	20	2
210–239	110	92	16	2
240–269	105	93	12	--------
270–299	103	94	7	2
300–329	98	91	7	--------
330–359	96	88	7	1
360–449	87	80	5	2

The cumulative percentage of success and failure at the end of 12 to 15 months' observation, by diagnosis and combined total, is given in figure 6.

Fifteen of the 137 patients treated are classified as treatment failures. These consist of 7 cases of clinical relapse, 6 of serologic relapse, 1 seroresistant, and 1 probable reinfection. The pretreatment diagnoses in these 15 patients were 2 primary seronegative, 6 primary seropositive, and 7 secondary syphilis.

One hundred and fourteen patients had positive pretreatment serologic titers, of which 88 reversed to seronegativity sometime within the 15 months. The median number of days required for the group was 100.5 days; for primary syphilis, 87 days; for secondary syphilis, 108 days. Forty (45.5 percent) of the 88 patients reached seronegativity within 3 months, and 75 (85.2 percent) within 6 months. Seven (8.0 percent) of the patients attaining seronegativity were later re-treated for clinical or serologic relapse.

The seronegativity rate was 81.9 percent at the end of the 12 to 15 months' observation period.

Of 135 patients having pretreatment cerebrospinal fluid examinations, 15, or 11.1 percent, had abnormal findings. Eight of the 15 patients were reexamined from 3 to 15 months following treatment; 6 showed normal and 2 abnormal, but improved, cerebrospinal fluids.

All reactions observed in this group of 137 patients were of a mild and transitory nature.

Table 10 lists the reactions in the 137 patients completing this treatment routine, grouped by prefever, fever, and postfever periods. In the prefever period (penicillin alone) 61 (44.5 percent) of 137 patients exhibited a Herxheimer reaction (primary fever and/or cutaneous manifestations). During fever, 68 patients of 137 manifested 84 reactions. The high incidence of gastrointestinal disturbance and dehydration was in great part due to the combined administration of arsenicals and fever. Under identical conditions but without arsenic (part II) these reactions had been noted to occur with less frequency. Fifty-eight patients exhibited 70 reactions in the postfever period. Twelve patients showed mild evidence of transient hepatic or nephritic involvement as was evidenced by a temporary rise in the icterus index and/or the appearance of albumin or red blood cells in the urine or in the blood nonprotein nitrogen. Eighteen patients developed herpes simplex.

Four patients (not included in table 10) developed reactions during fever which necessitated discontinuing treatment. Treatment was terminated for three of these because of dehydration and cardiovascular fatigue. The fourth patient was

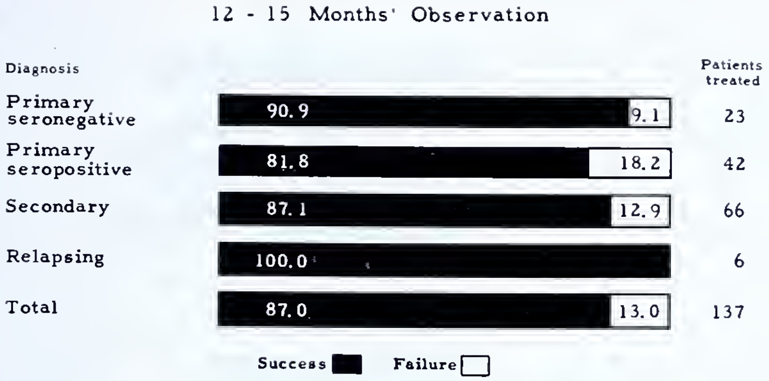

FIGURE 6.—Early syphilis patients treated with fever, mapharsen, bismuth, and penicillin. Cumulative percentages of successes and failures, 12 to 15 months' observation.

removed from the cabinet at the end of 1 hour and 15 minutes when the cardiac rate failed to show a corresponding increase to the rise in body temperature. The four patients rapidly responded to routine management.

Table 10.—*Early syphilis patients treated with fever, mapharsen, bismuth, and penicillin, by treatment reactions*

Period and type of reaction	Incidence		Patients
Prefever:			
Herxheimer		61	61
During fever:		84	68
Dehydration	27		
Gastrointestinal disturbances	44		
Cardiovascular fatigue	9		
Overhydration	1		
Hyperpneic tetany	2		
Hyperpyrexial psychosis	1		
Postfever:		70	58
Gastrointestinal disturbances	37		
Nephritic syndrome	8		
Hepatic syndrome	4		
Herpes simplex	18		
Other	3		

The combined total cumulative failure rate of 13.0 percent in the 12 to 15 months' observation period represents the lowest failure rate of all those schedules employed at this center and thus far evaluated for primary and secondary syphilis. It is believed that an analysis of the various factors involved is apropos. Evidence can be presented to show that the results obtained could not have been achieved from any one single factor.

Earlier investigators conducting experiments with early syphilis presented evidence to show that fever-therapy or chemotherapy alone could not have produced the results (*24, 25*).

Figure 7 compares the cumulative failure rates of patients having darkfield-positive lesions of secondary syphilis treated with schedules involving one or more of the factors comprising the present schedule and followed for a period of 12 to 15 months.

Two million four hundred thousand units of aqueous penicillin alone in 7½ days revealed a failure rate of 26.8 percent (*40*) : 5,000,000 units of penicillin in oil and beeswax, administered by one daily injection of 500,000 units for 10 days, resulted in a failure rate of 20.7 percent (*48*). When 10 and 25 million units of penicillin were administered intravenously over a period of 24 hours, the failure rates were 77.4 and 42.3 percent respectively (*39*). It can reasonably be concluded therefore that regardless of the penicillin absorption factors, the route of administration, the quantity of penicillin, or the time factor as employed in these schedules, penicillin alone could not account for the results of the schedule reported. As far as is known, no treatment schedules have been employed using the small amount of arsenical and bismuth alone, as was used in the treatment schedule reported here and therefore cannot be utilized for the purpose of comparison. However, there had been employed identical amounts of mapharsen and bismuth combined with 8 hours of fever at 106° F. rectal temperature, with a resulting 29.0-percent failure rate (part I). This then

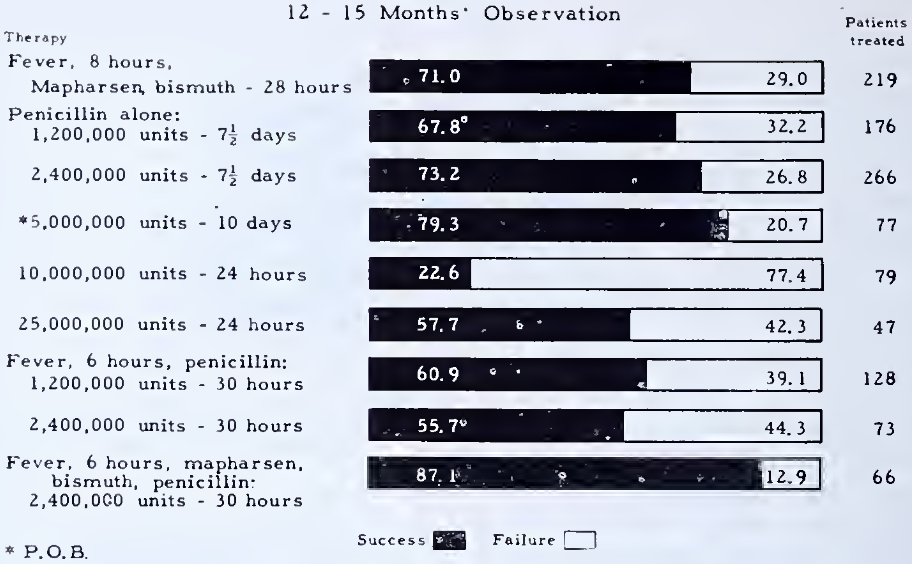

FIGURE 7.—Secondary syphilis darkfield-positive patients treated at the Chicago Intensive Treatment Center. Cumulative percentages of successes and failures, 12 to 15 months' observation.

would suggest that the superior results obtained in the present schedule were due to the addition of 2.4 million units of penicillin. That the combination of penicillin and fever alone is not responsible for these results is indicated by the two treatment schedules employing 1.2 million units (*43*) and 2.4 million units (part II) of penicillin and 6 hours' fever in 30 hours with failure rates of 39.1 and 44.3 percent, respectively.

It may be reasoned that when all variables are considered—time, dosage, combination of treatment modalities—one is dealing with several agents (fever, arsenical, bismuth, and penicillin), which when combined are productive of a higher index of therapeutic effectiveness.

Summary

1. One hundred thirty-seven patients with darkfield-positive lesions of early syphilis were given fever, mapharsen, bismuth, and penicillin in a treatment period of 30 hours.

2. Evidence is presented to show that these agents act synergistically.

3. The cumulative failure rate for the total group of 137 darkfield-positive early syphilis patients at the 12 to 15 months' observation period was 13.0 percent.

4. No serious reactions were observed.

5. Results of this treatment schedule present clinical evidence that early infectious syphilis may be effectively treated in 30 hours.

Conclusion

1. Authorities in venereology have long sought methods which would quickly, safely, and efficiently make the spreaders of syphilis noninfective. Out-patient clinic methods have not been successful in that even short 10- and 15-day penicillin-in-oil-and-beeswax schedules have shown that 13 to 17 percent of the patients, respectively, failed to complete their prescribed course of treatment. This failure has been a very serious shortcoming in all out-patient schedules and was indeed the father of the invention of rapid treatment centers.

2. After 20 years of constantly enlarging experience with physically induced fever, a successful method has been developed in which the majority of early syphi-

lis patients treated have been rendered noninfectious and thus removed as a public health menace.

3. The advantages of the treatment schedule employing fever, mapharsen, bismuth, and penicillin over the usual penicillin schedules are: first, the much higher therapeutic effectiveness; secondly, the obvious advantage of rapidity of treatment; and, thirdly, reduced patient resistance to hospitalization.

4. The treatment schedule has safety as attested by the lack of any serious reactions. Special training is required to administer artificial-fever therapy. The prevention of serious reactions is achieved by those who exercise the greatest diligence and care. More important than the type of apparatus selected for the administration of artificial-fever therapy is the skill and devotion of the physicians and nurse-technicians who engage in this specialized work.

5. It is hoped that this report will motivate others to confirm or refute the promising results of this study. New schedules employing the same therapeutic agents are now under way, aimed at reducing the failure rate still further, and will be the subject of a subsequent report.

6. Posttreatment observation of the patients in this investigation is to be continued.

Appendix

I

The percentages used for the figures on successes and failures were obtained by assuming that patients lost from observation would have shown the same ratio of results of treatment as those observed. The ratio of the number of patients observed in each period to the number observed in the preceding period was applied to the cumulative failure figure. Patients with positive significant titers (four Kahn units or more) after 12 to 15 months' observation have been grouped with failures. Those who were seronegative or who maintained nonsignificant titers (three Kahn units or less) were, for the present, considered successes. The same statistical method applies to the figures for 2 and 3 years' observation. This method of evaluation is considered rigid and, as a consequence, the failure rate tends to be relatively higher than similar studies utilizing less rigorous criteria.

II

Criteria for normal cerebrospinal fluid: Kahn, negative; cell count, 7 lymphocytes or less; total protein, 45 mg. percent or below; colloidal gold test, negative.

III

The results presented in this paper must be interpreted in light of the fact that from June 1943 to the present time commercial penicillin has been a changing mixture of various substances. The content of "impurities" has gradually decreased as potency, in terms of units per milligrams, has increased. The relative amounts of the several identified penicillin fractions, G, F, X, and K, have likewise varied from time to time. These two changes, and perhaps others, suggest that therapeutic efficacy may not have remained constant and that it may be significantly different today than it was originally. It is not now possible to assess the extent to which these changes may have affected the results here reported.

Acknowledgment

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CURRENT LITERATURE

NOTE: Abstracts of any article listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

ACTA OPHTH., COPENHAGEN

Luetic keratitis caused by an operation. Victor Larsen. 25: 195–199, 1947. [Abstracted in Am. J. Ophth., Chicago, 31: 1040, Aug. 1948.]

ACTA PATH. ET MICROBIOL. SCANDINAV., COPENHAGEN

How are we to reveal an unspecific positive Wassermann reaction? A. Lindau. Papers read before the Congress, July 7th–9th, 1947. Transactions of the Eighth Scandinavian Pathological Congress, Uppsala, July 7th–9th, 1947. 25: 14–16, Fasc. 1–2, 1948.

Problems concerning the estimation of the chemosensitivity of microbes and measuring of penicillin and streptomycin concentrations in the blood and spinal fluid. K. A. Jensen and Inger Kiaer. Papers read before the Congress, July 7th–9th, 1947. Transactions of the Eighth Scandinavian Pathological Congress, Uppsala, July 7th–9th, 1947. 25: 146–151, Fasc. 1–2, 1948.

Bordet-Wassermann's reaction carried out with cardiolipin-lecithin-cholesterol antigen. A preliminary report. Th. M. Vogelsang. Papers read before the Congress, July 7th–9th, 1947. Transactions of the Eighth Scandinavian Pathological Congress, Uppsala, July 7th–9th, 1947. 25: 167–174, Fasc. 1–2, 1948.

AM. J. M. SC., PHILADELPHIA

On the significance of abnormal forms of the ballistocardiogram. A study of 234 cases with 40 necropsies. [Syphilis] Isaac Starr and Robert L. Mayock. 215: 631–650, June 1948.

The renal elimination of caronamide (4′-carboxyphenylmethanesulfonanilide). Harold M. Peck, Elizabeth K. Tillson, William S. Waller and Karl H. Beyer. Physiology. Proceedings of the Physiological Society of Philadelphia, Session of Feb. 17, 1948. 216: 114, July 1948.

The morphological backgrounds of "genuine lipoid nephrosis." [Syphilis] Eli Moschowitz. 216: 146–157, Aug. 1948.

The clinical uses of intravenous diphenhydramine hydrochloride (benadryl hydrochloride). [VD] Morris H. Rosenberg and Lester S. Blumenthal. 216: 158–162, Aug. 1948.

AM. J. M. TECHNOL., LAFAYETTE

A plan to find the titer of an anticomplementary blood serum or spinal fluid. Charles E. Oates. 14: 93–98, Mar. 1948.

Kolmer cardiolipin complement-fixation test. Dorothy Patras. Symposium: Cardiolipin. 14: 159–162, May 1948.

The VDRL test. Margaret Anderson. Symposium: Cardiolipin. 14: 162–165, May 1948.

Notes on the VDRL test. Symposium: Cardiolipin. 14: 165–167, May 1948.

Notes on Kline cardiolipin tests. [As of February 29, 1948.] Symposium: Cardiolipin. 14: 167–168, May 1948.

Recent observations in the serology of syphilis. Margaret Zwally. 14: 224–227, July 1948.

Recent developments in special staining technics. [Syphilis] Mary Frances Gridley. 14: 347–350, Nov. 1948.

AM. J. MED., NEW YORK

Application of a quantitative gonococcal complement fixation test to the diagnosis of acute polyarthritis. Max Michael, Jr. [American Federation for Clinical Research. Abstracts: Southern Sectional Meeting, New Orleans, Jan. 26, 1948.] 5: 319–320, Aug. 1948.

Lymphogranuloma venereum of supraclavicular lymph nodes with mediastinal lymphadenopathy and pericarditis. Walter H. Sheldon, Margaret Wall, John R. Slade and Albert Heyman. [American Federation for Clinical Research. Abstracts: Southern Sectional Meeting, New Orleans, Jan. 26, 1948.] 5: 320, Aug. 1948.

Am. J. Ophth., Chicago

Optic neuropathies: a simplified classification and outline for etiologic diagnosis. [Syphilis] Alan C. Woods. 31: 1053–1069, Sept. 1948.

The use of bacitracin in ocular infections. Part I. Tolerance and permeability in the rabbit eye. Part II. Bacitracin therapy of experimental and clinical ocular infections. John G. Bellows and Chester J. Farmer. 31: 1070–1073, Sept. 1948; 1211–1216, Oct. 1948.

Analyst, Cambridge

Penicillins. Microchromatographic detection of different penicillins in a mixture. R. R. Goodall and A. A. Levi. 72: 277, 1947. [Abstracted in Quart. J. Pharm. & Pharmacol., London, 21: 85–86, Jan.–Mar. 1948.]

Ann. de dermat. et syph., Paris

General manifestations of lymphogranuloma venereum. (Manifestations générales de la maladie de Nicolas et Favre.) P. Le Coulant. 8: 5, 1948. [Abstracted in Brit. J. Ven. Dis., London, 24: 134, Sept. 1948.]

Ann. d'ocul., Paris

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Arch. Dermat. & Syph., Chicago

Spot test for syphilis. Using the modified Meinicke antigen of Ford Robertson and Colquohoun. R. F. Lane. 57: 802–809, May 1948.

Some obscure and paradoxic problems of syphilis. U. J. Wile. 57: 815–821, May 1948.

Syphilis of the central nervous system. Effect of quinacrine hydrochloride on the incidence of convulsions. William J. Welch, Eli Bauman and Peter Knowlton. 57: 868–872, May 1948.

Streptomycin therapy for chancroid. Ernest Jawetz. Clinical notes. 57: 916–918, May 1948.

Better Times, New York

All-out drive starts here against VD, 30: 1, Nov. 12, 1948.

Boll. d'ocul., Bologna

Bacteriologic and clinical investigations concerning the action of streptomycin on conjunctivitis due to gonococci, Koch-Weeks bacilli, diplobacilli, and on epidemic keratoconjunctivitis. D. Panzardi and G. Pasca. 26: 581–589, Sept. 1947. [Abstracted in Am. J. Ophth., Chicago, 31: 883–884, July 1948.]

Bratisl. lek. listy, Bratislava

Sudden blindness in a patient suffering from a cerebral tumor and cerebral syphilis. K. Trávik. 28: 210–215, 1948. [Abstracted in Am. J. Ophth., Chicago, 31: 1189, Sept. 1948.]

Brit. J. Ven. Dis., London

The treatment of neurosyphilis with penicillin. James Purdon Martin. 24: 89–100, Sept. 1948.

Gangrene of the toes in syphilis. Description of a case with a critical review of the literature. E. J. Moynahan. 24: 104–108, Sept. 1948.

Non-bacterial infection of the urinary tract. Waldemar E. Coutts. 24: 109–123, Sept. 1948.

Bull. et mém. Soc. méd. d hôp. de Paris, Paris

Portée pratique des réactions sérologiques syphilitiques positives apparaissant aprés vaccination jennerienne (réactions dites "faussement positives biologiques"). [Positive serum reactions for syphilis following vaccination (so-called biologic false positive reactions).] H. Perrot. nos. 5/6: 124–128, 1948. [Abstracted in Bull. Hyg., London, 23: 499, July 1948.]

Bull. Soc. méd. Hôp., Paris

Penicillin treatment of a case of amaurotic tabes with improvement. [Traitement par la pénicilline d'un cas de tabes amaurotique. Amélioration.] G. Guillain, J. Lereboullet, E. Sevileano and P. Strauss. 4: 773, 1947. [Abstracted in Brit. J. Ven. Dis., London, 24: 125, Sept. 1948.]

Cerebral accidents during penicillin treatment of a case of general paresis. [Accidents encéphalitiques graves au cours du traitement par la pénicilline du'un cas de paralysie générale.] J. Lereboullet and H. Sapin-Jalloustre. 4: 775, 1947. [Abstracted in Brit. J. Ven. Dis., London, 24: 125, Sept. 1948.]

Bull. U. S. Army M. Dept., Washington

Recommended changes in the treatment of early and latent syphilis. News and Comment. 8: 924, Nov. 1948.

Compt. rend. Acad. d. sc., Paris

Penicillin and streptomycin, rapid estimation of. G. Sanchez and A. Lamensans. 224: 1189, 1947. [Abstracted in Quart. J. Pharm. & Pharmacol., London, 21: 179–180, Apr.–June 1948.]

Indian J. Ven. Dis., Bombay

Control and prevention of venereal diseases. V. Govindan Nair. 15: 95–121, July–Sept. 1948.

J. Am. Pharm. A. [Scient. Ed.] Washington

A new absorption delaying vehicle for penicillin. F. H. Buckwalter and H. L. Dickson. 37 : 472–474, Nov. 1948.

J. Bact., Baltimore

*The nutritional requirements of treponemata. I. Arginine, acetic acid, sulfur-containing compounds, and serum albumin as essential growth-promoting factors for the Reiter treponeme. Harry Eagle and Harry G. Steinman. 56 : 163–176, Aug. 1948.

The nutritional requirements of treponemata. I. Arginine, acetic acid, sulfur-containing compounds, and serum albumin as essential growth-promoting factors for the Reiter treponeme. Harry Eagle and Harry G. Steinman. J. Bact., 56 : 163–176, 1948.

A report on the study of the nutritional requirements of the cultivable Reiter strain is presented in the hope that such data may offer clues to the growth requirements of the more pathogenic *Treponema pallidum.* The substances known to be essential for growth under the conditions of the experiments undertaken were arginine, acetic acid, any one of a series of compounds containing either free sulfhydryl groups or sulfur groups that could be reduced to the sulfhydryl form, and crystalline serum albumin.

The culture fluid used at the start of the investigation was composed of Brewer's thioglycolate medium and sterilized rabbit or human serum. A variety of substances was then assayed for their ability to permit multiplication of the organisms when added to the otherwise quantitatively inadequate basal medium. These compounds were made up at neutral pH in isotonic concentration. Direct microscopic counts were made after 4 to 6 days, at the peak of the growth curve.

The experimental results showed that the addition of arginine had a striking effect. The smallest concentration with a significant effect on growth was 0.0005 M, but beyond that level the number of organisms increased in proportion to the concentration of arginine. Of 43 amino acids and related compounds studied, arginine alone was essential for the growth of the Reiter strain. The initial inoculum throughout was 2 million organisms per milliliter; with arginine there were 116 million per milliliter after 6 days, while the counts for the other substances tested varied between 0 and 9 million per milliliter.

It was found that the necessary growth factor present in the dialyzable fraction of serum could be replaced by acetic acid. The smallest concentration exerting a significant effect was 0.0036 M, but the amount of growth increased with the concentration of sodium acetate to reach a maximum at 0.06 M. Unlike arginine, acetic acid was not unique in its growth-promoting activity, since a qualitatively similar effect was obtained with at least 15 of the 37 related compounds tested. The nondialyzable residue essential for the growth of the Reiter spirochete was found to be replaceable with crystalline bovine serum albumin. The minimum noticeable concentration was 0.1 percent. Of the sulfur-containing compounds tested, cysteine was found to be the most effective, although it, too, was not unique in its growth-promoting action. The phosphate buffer used in these experiments served only to maintain a suitable pH range and otherwise had no beneficial action.

In summary, five components have been identified as essential and in themselves adequate for the multiplication of the Reiter treponeme in an anaerobic enviroment; namely, arginine, acetic acid, any one of a number of sulfur-containing compounds, crystalline serum albumin, and an as yet unidentified component in the thioglycolate medium.

J. Florida M. A., Jacksonville

The diagnosis of secondary syphilis. John A. Barger. 35 : 298–299, Nov. 1948.

J. Immunol., Baltimore

Ultraviolet absorption spectroscopy of immune precipitates. Herman N. Eisen. 60 : 77–83, Sept. 1948.

*The serologic relationships between five cultured strains of supposed *T. pallidum* (Noguchi, Kroó, Nichols, Reiter and Kazan) and two strains of mouth treponemata. Harry Eagle and Frederick G. Germuth, Jr. 60 : 223–239, Oct. 1948.

The serologic relationships between five cultured strains of supposed *T. pallidum* (Noguchi, Kroó, Nichols, Reiter and Kazan) and two strains of mouth treponemata. Harry Eagle and Frederick G. Germuth, Jr. J. Immunol., 60: 223–239, 1948.

The serologic relationships between five purported strains of *Treponema pallidum* are studied through the cultivation of the organisms and their properties, the method of immunization, the test for immunity to virulent treponemata, and the agglutination and complement-fixation tests.

The data reported raise further doubts as to the propriety of identifying as *T. pallidum* the presently available cultured strains of treponemata, despite their supposed isolation from syphilitic lesions. None are pathogenic for rabbits, and all differ morphologically from the organisms as seen in lesions. All strains studied caused the formation of specific agglutinins and complement-fixing antibodies in high titer on injection into rabbits, but the rabbits did not develop a positive Wassermann or flocculation test even after injection with a total of 11 to 20 billion organisms administered over a period of 3 to 5 weeks. Rabbits immunized with these cultured organisms and later inoculated with pathogenic *T. pallidum* developed a primary lesion after a normal incubation period.

On the basis of their cross reactivity in agglutination and complement-fixation tests with rabbit antiserums, these five strains of cultivated treponemata fell into three distinct groups: (1) the Nichols and Noguchi strains were serologically indistinguishable; (2) the Reiter and Kazan strains cross reacted but were not identical; (3) the Kroó strain was serologically distinct from the other four. The Reiter strain was shown to be serologically almost identical with two strains of saprophytic mouth treponemata.

The data reported indicate that the five cultivated strains, all purporting to be *T. pallidum*, differ materially in their morphologic and antigenic properties from the pathogenic organism. The validity of their identification as *T. pallidum* is therefore questionable, according to the authors.

J. LAB. & CLIN. MED., ST. LOUIS

- Studies on cardiolipin antigen. IV. Variations in sensitivity of different lots of purified lecithin. Reuben L. Kahn and Elizabeth B. McDermott. 33: 1220–1223, Oct. 1948.
- *Studies on cardiolipin antigen. V. Standardization of antigen for the Kahn test. Elizabeth B. McDermott and Reuben L. Kahn. 33: 1224–1231, Oct. 1948.
- Procaine penicillin; therapeutic efficiency and a comparative study of the absorption of suspensions in oil and in oil plus aluminum monostearate and of an aqueous suspension containing sodium carboxymethylcellulose. Jay A. Robinson, Harold L. Hirsh, Bernard Milloff and Harry F. Dowling. 33: 1232–1240, Oct. 1948.
- Acquired resistance of psittacosis virus to sulfadiazine and effects of chemical antagonists on sulfonamide activity. [Lymphogranuloma venereum] Orvill J. Golub. 33: 1241–1248, Oct. 1948.

Studies on cardiolipin antigen. V. Standardization of antigen for the Kahn test. Elizabeth B. McDermott and Reuben L. Kahn. J. Lab. & Clin. Med., St. Louis, 33: 1224–1231, 1948.

This article deals with various aspects of the standardization of cardiolipin antigen for the standard Kahn test. Preliminary studies indicate that it behaves essentially like Kahn antigen in its titration with salt solution and in the final standardization of cardiolipin antigen for use with serum.

The three steps necessary for the standardization of tissue extract antigen are: (1) The titration of the antigen with salt solution to determine the titer at which the antigen is to be mixed with salt solution in the preparation of the antigen suspension for use with serum; (2) comparative tests with syphilitic and nonsyphilitic serums, employing standard antigen as a control, to determine how closely a new antigen behaves like standard antigen in sensitivity and specificity; (3) adjustment or correction of the new antigen if in its behavior with serums it is either oversensitive or undersensitive as compared with standard antigen.

Various ratios of lecithin-cardiolipin were tried in attempting to develop a workable cardiolipin antigen formula for the standard Kahn test. The use of a 25 : 1 ratio with a small amount of mastic was found to be unsuitable. A 10 : 1 ratio of lecithin-cardiolipin was found to be suitable as a working base, provided the concentration of these reagents was taken into consideration. The basic cardiolipin antigen formula employed was 1.0 percent purified lecithin, 0.1 percent cardiolipin, and 0.025 percent cholesterol.

The titration picture of the two antigens is similar. Cardiolipin antigen exhibits a narrow titration range with salt solution, while Kahn antigen exhibits a relatively wide titration range. The difference between Kahn and cardiolipin antigen is based on the probability that Kahn antigen contains nonantigenic colloids which are protective in nature, while cardiolipin antigen, because of its high purity, lacks these protective colloids.

The sensitivity of different lots of cardiolipin antigen varies, but it was observed that a standard level can be achieved by altering the ratio of lecithin-cardiolipin. It is believed that while modification of the lecithin-cardiolipin ratio will not, by itself, correct all undersensitive cardiolipin antigens, it is likely that a small change in the titer, such as a slight reduction in the amount of salt solution in the preparation of the antigen suspension, will increase sensitivity.

J. M. A. GEORGIA, ATLANTA

*Streptomycin in the therapy of granuloma inguinale. Report of 100 cases. Calvin H. Chen, Robert B. Greenblatt and Robert B. Dienst. 37 : 373–375, Oct. 1948.

Streptomycin in the therapy of granuloma inguinale. Report of 100 cases. Calvin H. Chen, Robert B. Greenblatt and Robert B. Dienst. J. M. A. Georgia, Atlanta, 37 : 373–375, 1948.

The authors report on a study of 100 Negro patients with granuloma inguinale, of 2 weeks' to 20 years' duration, treated with streptomycin at the University of Georgia School of Medicine over a 1½-year period. Of these patients, 67 had received some form of unsatisfactory treatment with antimonial preparations, and 33 had received no specific medication prior to admission. Eighty percent of the individuals in this study have been followed from 2 to 18 months.

The streptomycin used was dissolved in distilled water containing 20 to 30 percent of a 1-percent procaine hydrochloride solution and was injected intramuscularly in divided doses every 4 hours. The patients were divided into three groups regardless of their previous medication and duration of the disease.

Group I consisted of 32 patients treated with a daily dosage of 0.3 to 2.0 gm. of streptomycin for 6 to 62 days, with an average of 22 days. The response of the patients was slow. Donovan bodies often persisted for 10 days, and lesions took many weeks to heal. Two patients failed to respond to treatment and later became streptomycin resistant. There were six recurrences in this group.

Group II was comprised of 61 patients treated with a uniform dosage schedule of 4 gm. of streptomycin daily for 5 days. Improvement was usually noticed as early as 24 hours. Symptoms were usually completely alleviated after 48 hours, and Donovan bodies showed disintegration and decrease in number, completely disappearing after 5 days in the majority of patients. Complete healing with depigmented cicatrization was seen in 1 to 2 weeks. There were 4 recurrences and no primary failures.

Group III had seven patients with extensive lesions who received 4 gm. of streptomycin per day for 6 to 10 days. There were no primary failures or recurrences in this group. Seven recurrences from groups I and II were retreated successfully with 4 gm. of streptomycin per day for 5 to 10 days.

The authors recommend a 5-day course of treatment with 4 gm. of streptomycin in divided doses as the most effective treatment for granuloma inguinale. However, a 10-day course of treatment is preferred for patients with very extensive lesions or in cases of less prompt clinical and microscopic response.

Announcement

On April 7–8, 1949, there will be held in Washington, D. C., a joint meeting on venereal disease research. On Thursday, April 7, the program will be devoted to a Symposium on Recent Advances in the Study of Venereal Diseases under the auspices of the Syphilis Study Section, National Institutes of Health, Public Health Service, Federal Security Agency.

On Friday, April 8, the second day of the meeting, there will be held the annual scientific session of the American Venereal Disease Association. The business meeting of this Association (limited to members) will be held on the night of April 7, 1949. The time and place of this meeting will be announced later to the membership.

The program for each day will be held in room 1517, Federal Security Building North, beginning at 10 a. m.

All persons interested in this phase of medicine are cordially invited to attend the meeting. Copies of the program will be sent at a later date upon request.

All inquiries should be addressed to: Mr. Francis L. Schmehl, Executive Secretary, Syphilis Study Section, Division of Research Grants and Fellowships, National Institutes of Health, Bethesda 14, Md., or to Dr. William L. Fleming, Secretary, American Venereal Disease Association, 750 Harrison Avenue, Boston, Mass.

First Report on Out-Patient Case Holding in Virginia

During a 9-month period, September 1, 1947, to June 30, 1948, 3 areas in Virginia—Alexandria, Arlington County, and Richmond, with a population of 72,000, 123,832, and 228,400, respectively—kept a record of the attendance of syphilis patients treated in clinics on an out-patient basis. The schedule of treatment was 600,000 units of penicillin (POB) daily for 6 days. However, a patient was considered to have completed treatment satisfactorily if he received a total of 3,600,000 units within 12 days. Of the 513 patients who began treatment, only 23 failed to complete this schedule in the prescribed manner, resulting in a "case-holding failure rate" of 4.5 percent. There were about as many male as female patients, but the nonwhite predominated 10 to 1.

Seventy-four percent of the patients kept all appointments and completed treatment within 6 days. Thirteen percent completed treatment in 7 days, 5 percent in 8 days, and approximately 4 percent took 9 to 11 days. Of the 23 patients who failed to complete treatment, 4 moved away, 3 had pregnancy complications, 2 were ill, 2 had treatment reactions, and 2 were quarantined; for the remaining 10, no reason was given. However, of the 23 "case-holding failures," 11 later received adequate treatment on an out-patient basis, 4 were hospitalized and treated, and the remaining 8 apparently did not receive any subsequent treatment.

The project is a continuing one, and later reports will be made.

STATISTICS

Cases of Syphilis and Gonorrhea Reported to the Public Health Service by State and Territorial Health Departments, First Quarter Fiscal 1949

[Known military cases excluded]

Federal Security Agency regions	Syphilis															Gonorrhea		
	Primary and secondary			Early latent			Late and late latent			Congenital			Not stated					
	Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter	
		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources
Region 1—Total	256	0.78	0.83	200	0.71	0.62	636	0.90	0.85	63	0.85	1.24	109	0.89	0.77	1,358	1.15	1.31
Connecticut	33	.63	.67	77	.84	.75	124	.84	.80	17	([a])	([a])	37	1.03	.79	302	1.20	1.01
Maine	62	.95	1.09	24	.71	.27	52	1.08	.77	2	([a])	([a])	3	([a])	([a])	95	.90	1.68
Massachusetts	110	.80	.87	67	.60	.59	296	.88	.86	30	.91	([a])	0	-------	-------	717	1.11	1.49
New Hampshire	19	([a])	([a])	7	([a])	([a])	24	.80	.86	3	([a])	([a])	1	([a])	([a])	53	.91	.98
Rhode Island	23	.74	([a])	22	.76	.67	137	1.05	1.05	8	([a])	([a])	38	.88	.73	93	1.29	.81
Vermont	9	.36	.36	3	([a])	([a])	3	([a])	([a])	3	([a])	([a])	30	.83	.81	98	1.96	1.96
Region 2—Total	1,849	.86	.81	3,420	.87	.83	6,202	.84	.85	368	.77	.78	190	.70	.69	11,842	1.05	1.15
Delaware	37	.58	.43	84	.65	.69	33	.23	.81	2	([a])	([a])	47	1.09	([a])	87	1.53	1.35
New Jersey	303	.97	.92	913	1.17	1.04	1,143	1.02	1.14	49	.74	.63	20	([a])	([a])	1,518	1.25	1.34
New York	984	.85	.84	1,326	.74	.77	4,104	.82	.80	179	.69	.79	85	.49	.47	7,616	1.01	1.11
New York City	780	.80	.74	1,207	.71	.72	3,060	.77	.73	133	.70	.95	65	.43	.43	6,055	.99	1.10
Pennsylvania	525	.87	.62	1,097	.90	.66	922	.82	.75	138	1.01	([a])	38	1.00	.90	2,621	1.07	-------
Philadelphia[b]	214	.84	-------	817	1.06	-------	517	.84	-------	48	1.41	-------	5	.11	-------	2,392	1.25	-------
Pittsburgh[b]	127	1.14	-------	122	1.05	-------	168	1.01	-------	25	.96	-------	0	-------	-------	307	1.28	-------
Region 3—Total	2,343	.95	.89	2,670	.93	.86	2,574	1.03	.92	321	.93	.74	81	.78	.90	16,007	1.28	2.46
District of Columbia	245	1.11	.75	361	1.24	1.29	435	1.33	1.52	23	.85	([a])	0	-------	-------	5,174	1.67	[c] 16.53
Maryland	440	.94	.91	481	.93	.73	712	1.09	.83	80	1.31	([a])	42	.91	([a])	2,170	1.16	1.51
Baltimore	264	.84	.55	341	.89	.81	557	1.14	.97	51	1.82	([a])	40	1.11	([a])	1,679	1.13	1.53
North Carolina	738	1.01	.97	714	.92	1.00	288	1.14	1.96	93	.83	([a])	0	-------	-------	4,133	1.17	1.11
Virginia	555	.84	.80	781	.85	.73	594	.77	.77	70	.84	([a])	39	.67	([a])	3,288	1.16	1.16
West Virginia	365	.92	.97	333	.89	1.03	545	1.11	.95	55	.87	([a])	0	-------	-------	1,242	1.09	1.15
Region 4—Total	1,665	.88	1.31	2,717	.97	1.32	4,653	1.08	1.30	370	.91	1.21	446	.98	.94	7,230	1.14	1.16
Kentucky	362	.91	.88	340	.99	.88	489	1.05	1.08	42	1.05	([a])	15	.60	.50	1,778	1.19	1.03
Michigan	489	.93	1.10	554	.81	.91	1,344	.98	1.02	108	.81	1.11	431	1.01	.96	2,602	1.17	1.19
Ohio	814	.85	1.68	1,823	1.03	1.50	2,820	1.13	1.48	220	.95	1.32	0	-------	-------	2,850	1.08	1.15
Region 5—Total	1,245	.90	.88	1,561	.83	.82	2,634	.87	.85	263	1.08	1.05	3	1.50	1.50	9,025	1.12	1.03
Illinois	838	.89	.86	1,195	.85	.82	1,762	.88	.85	135	1.30	1.49	0	-------	-------	7,665	1.12	1.02
Chicago	524	.94	.96	840	.88	.83	993	.84	.79	73	1.16	([a])	0	-------	-------	6,157	1.15	1.07
Indiana	292	.84	.83	236	.78	.88	461	.89	1.06	91	.99	.88	2	([a])	([a])	766	1.15	1.15
Minnesota	44	1.26	1.31	39	.95	1.09	134	.99	.92	7	([a])	([a])	1	([a])	([a])	324	.86	.95
Wisconsin	71	1.20	.98	91	.65	.68	277	.75	.68	30	.73	.73	0			270	1.26	1.20

Region 6—Total	4,781	.95	.97	6,966	.94	.94	5,933	1.02	.89	1,130	.89	1.02	976	.61	.62	24,505	1.03	1.04
Alabama	702	.81	.83	1,701	1.11	1.28	1,160	.72	.90	108	.61	(a)	916	.60	.62	1,696	1.12	1.09
Florida	1,063	.80	.80	1,210	.99	.90	1,150	1.09	.92	177	1.21	1.00	1	(a)	(a)	4,228	.79	.86
Georgia	935	1.15	2.66	793	.86	(a)	778	1.09	1.07	165	1.04	--------	24	47	--------	4,444	1.10	(a)
Mississippi	682	.99	.84	963	.92	1.60	1,507	1.67	1.29	219	.77	(a)	0	--------	--------	2,801	1.00	1.01
South Carolina	704	1.13	1.31	746	.90	1.06	355	1.12	1.44	74	.90	(a)	0	--------	--------	2,372	1.00	(a)
Tennessee	538	.94	.68	622	.76	.70	593	.71	.69	75	1.00	(a)	28	(a)	(a)	6,171	1.08	1.18
Puerto Rico	156	.99	--------	917	.91	--------	382	1.03	--------	308	.90	--------	0	(a)	--------	2,777	1.41	--------
Virgin Islands	1	(a)	--------	14	(a)	--------	8	(a)	--------	4	(a)	--------	7	(a)	--------	16	.47	(a)
Region 7—Total	747	.90	.90	833	.92	.96	1,358	1.11	1.46	141	1.10	1.19	113	1.18	1.15	2,929	1.18	1.47
Iowa	98	1.05	1.85	94	.90	.89	145	1.51	2.12	18	(a)	(a)	0	(a)	(a)	375	1.49	2.29
Kansas	132	1.17	1.07	162	1.41	1.84	409	1.81	2.76	42	1.56	(a)	0	--------	--------	457	1.34	1.36
Missouri	407	.81	.70	466	.80	.76	657	.88	.98	59	.89	.90	54	1.15	1.22	1,680	1.10	1.18
St. Louis	180	.94	.74	237	.72	.53	331	.80	.84	20	.71	(a)	0	--------	--------	1,056	1.03	1.19
Nebraska	50	1.43	1.08	63	1.17	1.38	98	1.03	1.19	15	(a)	(a)	59	1.44	1.30	209	.92	.90
North Dakota	29	.66	.66	11	(a)	(a)	24	1.04	1.04	2	(a)	(a)	0	(a)	(a)	60	1.40	1.40
South Dakota	31	.78	(a)	37	1.19	(a)	25	.86	(a)	5	(a)	(a)	0	--------	--------	148	1.56	2.00
Region 8—Total	2,280	.87	.92	3,533	.87	1.00	4,828	.97	.89	943	.87	1.24	2,519	1.37	1.37	14,240	1.03	.99
Arkansas	389	.73	.84	1,128	1.08	1.10	2.531	1.00	.91	337	.88	1.00	7	(a)	(a)	1,483	1.06	1.05
Louisiana	624	.93	(a)	724	.78	(a)	649	1.00	.44	142	.81	(a)	450	1.22	1.04	3,653	1.04	.66
New Mexico	54	.68	.80	106	1.12	(a)	116	.85	(a)	29	1.26	(a)	0	--------	--------	301	1.15	.93
Oklahoma	291	1.05	1.27	375	.98	1.04	663	1.03	.96	93	1.16	1.52	42	.59	.58	1,860	1.10	.98
Texas	922	.88	.86	1,200	.74	.50	869	.88	.63	342	.82	(a)	2,020	1.46	1.46	6,943	.99	.99
Region 9—Total	211	.88	.93	179	.97	1.04	303	.96	.98	40	1.08	.96	17	.68	(a)	941	1.34	.95
Colorado	109	.93	.77	78	.91	1.06	120	.68	.61	17	(a)	(a)	0	--------	--------	578	1.39	.82
Idaho	20	.50	(a)	12	(a)	(a)	48	.98	(a)	6	(a)	(a)	11	.55	(a)	160	1.44	.70
Montana	44	1.22	1.07	40	1.38	(a)	60	1.30	1.29	8	(a)	(a)	4	(a)	(a)	89	2.17	(a)
Utah	18	.62	(a)	19	.83	(a)	44	1.57	(a)	8	(a)	(a)	0	--------	--------	83	.87	(a)
Wyoming	20	(a)	(a)	30	.88	.97	31	(a)	(a)	1	(a)	(a)	2	(a)	(a)	31	.82	1.10
Region 10—Total	1,123	.93	.98	1,494	1.03	.96	2,781	.90	.88	249	1.28	1.23	269	1.14	1.92	8,888	1.06	1.14
Arizona	65	.69	.46	106	.99	(a)	94	.60	.64	9	(a)	(a)	0	--------	--------	260	.90	1.23
California	819	.94	1.02	1,198	1.11	1.12	2,197	.95	.91	164	1.12	1.07	230	1.11	(a)	6,987	1.06	1.12
Nevada	22	.47	.31	0	--------	--------	107	.80	.95	6	(a)	(a)	0	--------	--------	179	1.10	.95
Oregon	73	1.26	1.45	37	.74	(a)	106	.62	.63	3	(a)	(a)	0	--------	--------	327	.91	1.52
Washington	119	1.07	1.17	125	.90	.69	199	.99	.82	27	(a)	(a)	24	.92	(a)	765	1.11	1.44
Alaska	15	(a)	(a)	12	.25	.25	22	.79	.79	10	(a)	(a)	12	(a)	(a)	123	1.02	1.02
Hawaii	10	(a)	(a)	16	.53	(a)	56	.68	.63	30	(a)	(a)	3	(a)	(a)	247	1.14	1.14
Canal Zone	7	(a)	--------	14	(a)	--------	49	1.26	--------	3	(a)	--------	0	--------	--------	172	1.23	--------
Continental United States	16,318	.91	.96	22,614	.92	.97	31,434	.96	.97	3,536	.91	1.04	4,701	.99	1.00	93,802	1.09	1.19
Total United States including Territories	16,507	.91	.96	23,587	.91	.96	31,951	.96	.97	3,891	.92	1.06	4,723	.99	1.00	97,137	1.09	1.19

[a] Ratio not calculated when base is less than 20.
[b] Data from VM-820.
[c] Intensive educational case-finding program and free penicillin distribution to co-operating physicians duing the first quarter 1949.

Source: Form 8958-B FSA—PHS—Division of Venereal Disease, Office of Statistics, 1/12/49 (MC-AS-TM) mjm.

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Volume 30 April 1949 Number 4

ORIGINAL ARTICLES

Penicillin in the Treatment of Syphilis in Pregnancy 95
H. N. Cole, M. D. Evan W. Thomas, M. D.
Frederick Plotke, M. D., M. P. H. Kenneth H. Jenkins, *Biostatistician*

A Quantitative Turbidimetric Method for the Determination of Spinal Fluid Protein 100
Hilfred N. Bossak, *Serologist*
Arthur A. Rosenberg, *Serologist*
Ad Harris, *Senior Serologist*

Preservation and Inoculation Studies on *Treponema Pallidum* . . . 104
Charlotte McLeod, Sc. D.
R. C. Arnold, *Senior Surgeon*

Out-Patient Attendance of Early Syphilis Patients Treated by Private Physicians in Vermont . , ... 107
R. B. Aiken, M. D.

CURRENT LITERATURE 109

CURRENT NOTES AND REPORTS

Educational Program at Alto Medical Center—Alto, Georgia . . . 120
Dorothy Johnston, *Assistant Nurse Officer (R)*

Public Health Nursing Fellowships 121

SYPHILIS MORTALITY—1900–47 123

FEDERAL SECURITY AGENCY
Public Health Service

899

Submission of Manuscripts

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Penicillin in the Treatment of Syphilis in Pregnancy

H. N. Cole, M. D.;[1] Frederick Plotke, M. D., M. P. H.;[2] Evan W. Thomas, M. D.;[3] and Kenneth H. Jenkins, Biostatistician, United States Public Health Service

The effectiveness of penicillin therapy for syphilis in pregnant women in preventing the transmission of the infection to offspring has been reported in recent studies (*1, 2, 3, 4*). However, most of these studies were made on small groups of cases treated for primary and secondary syphilis, leaving largely a matter of conjecture the results of penicillin treatment in latent cases. The present study of the pooled records of three large intensive treatment centers was initiated to investigate (1) whether penicillin treatment prevents the transmission of the disease from the mother to the fetus as effectively in cases of early latent syphilis as it does in primary and secondary cases, and (2) whether equally beneficial results can be expected from penicillin therapy regardless of the duration of pregnancy at the time treatment is administered.

For the purpose of uniformity, patients who were re-treated for reinfection, infectious relapse, serorelapse, or seroresistance prior to delivery were excluded from the study, since there were too few individuals in these groups for comparison. Inasmuch as the primary objective is an evaluation of the results of penicillin treatment in the prevention of congenital syphilis, the analysis is made on the number of the outcomes of pregnancy, rather than on the number of women treated.

Table 1.—*Distribution of pregnancy outcomes, by diagnosis of mother at time of treatment*

Diagnosis of mother at time of treatment	Outcomes of mothers treated during pregnancy	
	Number	Percent
Total	414	100.0
Primary syphilis	32	7.7
Secondary syphilis	253	61.1
Early latent syphilis	129	31.2

Table 1 presents the number and the percentage distribution of the outcomes, according to the diagnosis of the mother at time of treatment.

Of the 414 outcomes of mothers treated during pregnancy (table 2), 392 were live births and 22 were fatalities (including abortions, miscarriages, and stillbirths), a fatality rate of 56.1 per 1,000 live births. This rate compares favorably with the stillbirth rate, 80.9, released by the National Office of Vital Statistics, for the city of New York (1944), the only area in the United States requiring the reporting of all products of conception.

Table 2.—*Live births and fatal outcomes of pregnancies of women treated for syphilis*

Diagnosis of mother at time of treatment	Total		Live births		Fatal outcomes	
	Number	Percent	Number	Percent	Number	Percent
Total	414	100.0	392	94.7	22	5.3
Primary and secondary syphilis	285	100.0	269	94.4	16	5.6
Early latent syphilis	129	100.0	123	95.3	6	4.7

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[1] Department of Dermatology and Syphilology of Western Reserve Medical School and of the Cleveland City Hospital, in cooperation with John Rauschkolb, M. D., and Gerard DeOreo, M. D.

[2] Venereal Disease Control Officer, Chicago Board of Health.

[3] Director, Rapid Treatment Center, Bellevue Hospital, New York City.

In order to evaluate the results of penicillin therapy, a further classification was made of pregnancy outcomes on the basis of clinical and serologic status:

Group 1.—Confirmed nonsyphilitic outcomes: live births with negative serologic results after a minimum of 90 days' follow-up. Group 1 includes one child who died in less than 90 days on whom an autopsy showed no evidence of syphilis.

Group 2.—Confirmed syphilitic outcomes: the outcomes with a diagnosis of syphilis established through clinical evidence, serology, or autopsy.

Group 3.—Unconfirmed outcomes: outcomes whose status could not be established. These include live births with less than 90 days' postdelivery observation and fatal outcomes or neonatal deaths upon which no autopsy was performed.

Although most of the unconfirmed outcomes were probably nonsyphilitic, it was felt that a more accurate evaluation of the results of therapy could be presented if these results were based only on outcomes definitely established as syphilitic or nonsyphilitic by clinical and serologic evidence. For this reason, no attempt has been made to prorate the unconfirmed cases on the basis of the confirmed cases.

Table 3 presents the distribution of pregnancy outcomes by stage of infection in the mother at time of treatment. Table 4 shows a further break-down of the cases in the group of unconfirmed outcomes.

Table 3.—***Diagnostic status of outcomes of pregnancies of women treated for syphilis***

Diagnosis of mother at time of treatment	Total outcomes	Confirmed nonsyphilitic outcomes	Confirmed syphilitic outcomes	Outcomes with unconfirmed status
Total	414	300	11	103
Primary and secondary syphilis	285	207	9	69
Early latent syphilis	129	93	2	34

Table 4.—***Distribution of outcomes of unconfirmed status of pregnancies of women treated for syphilis***

Diagnosis of mother at time of treatment	Total outcomes	Live births		Fatal outcomes[1]
		Not observed within 90 days	Dead within 90 days	
Total	103	70	13	20
Primary and secondary syphilis	69	44	11	14
Early latent syphilis	34	26	2	6

[1] Abortions, miscarriages, and stillbirths.

From the data presented in table 5, it would seem that penicillin therapy is effective in preventing the transmission of syphilitic infection to the fetus irrespective of the stage of the disease in the mother at time of treatment. Of the 216 confirmed outcomes of pregnancy in primary and secondary syphilis treated during pregnancy, 9 (4.2 percent) were found to be syphilitic, while 2 (2.1 percent) of the 95 known outcomes in early latent cases were infected.

In terms of all live births, the indicated incidence of congenital syphilis is

Table 5.—***Distribution of confirmed outcomes of pregnancies of women treated for syphilis***

Diagnosis of mother at time of treatment	Total confirmed outcomes		Confirmed syphilitic outcomes		Confirmed nonsyphilitic outcomes	
	Number	Percent	Number	Percent	Number	Percent
Total	311	100.0	11	3.5	300	96.
Primary and secondary syphilis	216	100.0	9	4.2	207	95.
Early latent syphilis	95	100.0	2	2.1	93	97.

maximal because, of those babies who were examined following delivery but under observation for less than 90 days, only 1 out of 47 had positive serologic results at any time. Since none of the children in this study who were diagnosed as being syphilitic had a negative serologic reaction at any time, it would be fairly safe to assume that the majority of the remaining 46 would ultimately have been confirmed as being nonsyphilitic.

The patients in this study were treated with various schedules of therapy, in which the amount of aqueous penicillin administered ranged from 200,000 units to 9,600,000 units. One patient who did not complete the scheduled treatment and who received less than 600,000 units of penicillin delivered a syphilitic infant. Table 6 presents the distribution of pregnancy outcomes of patients by amount of penicillin received.

On the basis of the greater percentage of syphilitic outcomes occurring in the groups treated with smaller dosages of penicillin, it appears that better results are generally obtained from the use of treatment schedules employing at least 2,400,000 units of penicillin. It is to be noted, however, the high percentages of syphilitic outcomes are in schedules with small numbers of cases.

If all the cases, regardless of diagnosis, are divided between those who received less than 2.4 million units and those who received that amount or more, a noticeable difference exists between the two respective rates of syphilitic outcomes. The confirmed outcomes of the former group, receiving less than 2.4 million units, were syphilitic in 8.9 percent of the cases, while the figure for the latter group was 2.5 percent. The results appear to be strongly in favor of large amounts of penicillin, but the difference is not statistically significant at the 5-percent level.

On the basis of current reports, it is the general opinion that penicillin treatment for syphilis at any time during pregnancy is effective in preventing congenital syphilis. Within the limits of the data in this study, this statement appears to be true.

Table 6.—*Confirmed syphilitic and nonsyphilitic outcomes of pregnancies of women treated during pregnancy for syphilis, by amount of penicillin*

Schedule of therapy	Primary and secondary					
	Total confirmed outcomes		Confirmed nonsyphilitic outcomes		Confirmed syphilitic outcomes	
	Number	Percent	Number	Percent	Number	Percent
Total schedules	216	100.0	207	95.8	9	4.2
Less than 600,000 units	1	100.0	----------	0.0	1	100.0
600,000 units	11	100.0	11	100.0	----------	0.0
1,200,000 units	39	100.0	36	92.3	3	7.7
1,600,000 units	5	100.0	4	80.0	1	20.0
2,400,000 units	56	100.0	55	98.2	1	1.8
3,600,000 units	1	100.0	1	100.0	----------	0.0
4,000,000 units	28	100.0	27	96.4	1	3.6
4,800,000 units	66	100.0	65	98.5	1	1.5
9,600,000 units	9	100.0	8	88.9	1	11.1
	Early latent					
Total schedules	95	100.0	93	97.9	2	2.1
Less than 600,000 units	----------	----------	----------	----------	----------	----------
600,000 units	1	100.0	1	100.0	----------	0.0
1,200,000 units	3	100.0	2	66.7	1	33.3
1,600,000 units	1	100.0	1	100.0	----------	0.0
2,400,000 units	19	100.0	19	100.0	----------	0.0
4,000,000 units	20	100.0	20	100.0	----------	0.0
4,800,000 units	26	100.0	25	96.2	1	3.8
9,000,000 units	1	100.0	1	100.0	----------	0.0
9,600,000 units	24	100.0	24	100.0	----------	0.0

Forty-three patients were treated in the last month of pregnancy. The median date of starting the treatment of these 43 patients was 23 days before delivery. The latest was 6 days, with treatment completed after the delivery of a healthy child. Table 7 shows the percentage of outcomes that were diagnosed as syphilitic for each 3-month period (chosen for convenience) in which treatment was instituted. The highest rate of congenital syphilis appears in the first period for the primary and secondary stage, but this rate is not significantly different from the rates in the other two periods. There were only two infected outcomes from mothers with early latent syphilis, and both were in the third period. However, since 60 percent of the early latent cases were treated during these last 3 months, it is not too surprising that the two congenital syphilitic outcomes fall in that period. This point may not be too important, however, for when the number of syphilitic outcomes in the two groups (primary-secondary and early latent) are subjected to the Chi-square test for significance between the first 6 and the last 3 months, such a distribution of 11 cases could occur by chance 50 times out of 100.

Table 7.—***Distribution of confirmed outcomes, by stage of infection and duration of pregnancy of the mother at time of treatment***

Stage of infection and duration of pregnancy	Total confirmed outcomes		Confirmed nonsyphilitic outcomes		Confirmed syphilitic outcomes	
	Number	Percent (by trimester)	Number	Percent (by trimester)	Number	Percent (by trimester)
Primary and secondary:						
1 month	5	--------	4	--------	1	--------
2 months	10	100.0	9	91.4	1	8.6
3 months	20	--------	19	--------	1	--------
4 months	18	--------	17	--------	1	--------
5 months	37	100.0	36	97.7	1	2.3
6 months	33	--------	33	--------	--------	--------
7 months	40	--------	38	--------	2	--------
8 months	30	100.0	29	95.7	1	4.3
9 months	23	--------	22	--------	1	--------
Early latent:						
1 month	--------	--------	--------	--------	--------	--------
2 months	1	100.0	1	100.0	--------	0.0
3 months	3	--------	3	--------	--------	--------
4 months	8	--------	8	--------	--------	--------
5 months	10	100.0	10	100.0	--------	0.0
6 months	13	--------	13	--------	--------	--------
7 months	26	--------	24	--------	2	--------
8 months	14	100.0	14	96.7	--------	3.3
9 months	20	--------	20	--------	--------	--------

Table 8.—***The distribution of confirmed outcomes of pregnancy, by results of serologic tests for syphilis of the mother at time of delivery***

Original diagnosis and serologic reaction at time of delivery	Total confirmed outcomes	Confirmed nonsyphilitic outcomes	Confirmed syphilitic outcomes
Primary and secondary syphilis:			
Positive	140	[1] 131	[1] 9
Negative	65	65	--------
Unknown	11	11	--------
Early latent syphilis:			
Positive	77	75	2
Negative	10	10	--------
Unknown	8	8	--------

[1] Includes one fatal outcome.

In table 8, the serologic reaction of the mother at the time of delivery is considered in relation to the outcome of pregnancy. It is interesting to note that all the syphilitic outcomes were from mothers whose serologic tests had not attained negativity at the time of delivery.

Analysis of the data brought to light some observations which are noteworthy in the consideration of antisyphilitic treatment during pregnancy. Not all the children were tested in all the observation periods,[4] but it is interesting to note that of those who were seen in all four periods, all the infants who were positive in the second or later period were also positive in all preceding periods, and, once the serologic test showed negative results, there was no relapse to positive.

An analysis was made of the children in this study who showed a positive serologic test for syphilis on first examination following birth. Of the children tested at some time between the seventh and thirtieth days following birth, 63 percent of those with positive serologic results were eventually diagnosed as being nonsyphilitic. Among infants found to be positive in the second and third month, 56 percent and 21 percent, respectively, were found later to be nonsyphilitic. It is of further interest to note that all the nonsyphilitic children with positive results at any time came from mothers who were treated during the fifth or later month of that pregnancy. In all cases, the results of serologic tests of the mother were positive at the time of the last test prior to delivery. The children in whom the positivity persisted longest came from mothers treated for early latent syphilis. These findings, while not new, strongly support the belief that a diagnosis of congenital syphilis made on the basis of qualitative serologic tests alone may be premature if made before the child is 3 months old.

Although no attempt has been made to evaluate the results of penicillin therapy on the infection of the mother, it should be of interest, especially to the clinician, to observe the status of the mother following delivery in relation to the status of the outcome of pregnancy. All the 11 patients in this study whose pregnancies terminated in syphilitic infants relapsed following delivery. Thus, if the child is diagnosed as having congenital syphilis, the mother will in all probability relapse. However, relapse in the mother does not necessarily mean that the child will develop congenital syphilis, since only a third of all relapsing mothers had syphilitic outcomes. The median relapse date of mothers of syphilitic children was 150 days after delivery, while the median relapse date for mothers of nonsyphilitic children was 240 days after delivery.

The statements presented in this report are based on the pregnancy outcomes of patients treated for syphilitic infection whenever it was possible to determine the status of such outcomes through clinical and serologic evidence. In the absence of autopsy information, it was necessary to assign the greater number of the fatal outcomes to the unknown outcome category. This exclusion of so large a proportion of the fatalities might be questioned on the basis that it would tend to reduce the number of congenital syphilis cases reported in this group; however, the low fatality ratio found in this series, when compared with that for the city of New York, lends support to the belief that not all the fatal outcomes were due to syphilis.

Summary

1. This study was based on 414 outcomes of pregnancy from previously untreated patients given amounts of penicillin varying from 200,000 to 10,000,000 units.

2. A status based on clinical and serologic evidence was established at 90 days or later in 311 of the outcomes. It was found that 11 of those (3.5 percent) were diagnosed as syphilitic.

3. Of the 216 known outcomes of patients treated for primary and secondary infection, 4.2 percent were found to be syphilitic, while congenital syphilis was diagnosed in 2.1 percent of the outcomes of patients treated for early latent syphilis. These differences in rates point a direction but are not statistically conclusive.

4. Best results were obtained from treatment schedules employing at least 2,400,000 units of penicillin.

5. No syphilitic outcomes of pregnancy were noted in those mothers who had

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[4] Observation periods were arbitrarily set at (1) 7 to 30 days after birth; (2) 30 to 59 days; (3) 60 to 89 days; and (4) 90 days or more after birth.

attained a negative serologic test prior to delivery.

6. Nonsyphilitic infants with a positive serologic test sometime during the first 3 months of life, came from patients treated in the fifth month of pregnancy or later.

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A Quantitative Turbidimetric Method for the Determination of Spinal Fluid Protein[1]

Hilfred N. Bossak, Serologist, Arthur A. Rosenberg, Serologist, and Ad Harris, Senior Serologist, United States Public Health Service

Several methods for the estimation of total protein in spinal fluid have been reported (*1, 2, 3*). Those most widely used employ sulfosalicylic acid as a precipitating agent. In a preliminary study to determine the relative efficiency of this reagent, evidence was acquired indicating that changes in albumin-globulin ratio could have pronounced effects on estimated total protein values.

During the course of this investigation, a new procedure for the quantitative determination of total spinal fluid protein was evolved which was found to be minimally influenced by changes in albumin-globulin ratio. The purpose of this report is (1) to describe this new test procedure employing 10-percent trichloracetic acid as a protein precipitant and (2) to present the comparative findings obtained with this and the Denis-Ayer (*1*) sulfosalicylic acid method on prepared mixtures of albumin and globulin and on spinal fluids from selected donors.

Methods

Micro-kjeldahl analyses were performed by the direct nesslerization method of Wong (*4*), which employs 50-percent sulfuric acid for digestion and sodium persulfate for oxidation.

The Denis-Ayer turbidimetric procedure was performed in the usual manner for precipitating protein, by the addition of 5-percent sulfosalicylic acid solution. The turbidities thus obtained were measured by means of a photoelectric colorimeter[2] in terms of percent transmission, which in turn was converted to milligrams percent of total protein by reference to a calibration curve.

The 10-percent trichloracetic acid procedure as developed in this laboratory was performed as follows:

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[1] From the Venereal Disease Research Laboratory, U. S. Marine Hospital, Staten Island 4, N. Y. Medical Director J. F. Mahoney in charge. Presented before the annual meeting of the American Public Health Association in Boston, Mass., Nov. 9, 1948.

[2] Lumetron Clinical Photoelectric Colorimeter Model 400–A, Photovolt Corp., New York 16, N. Y.

1. Pipette 2.5 ml. of spinal fluid into a 13 x 100 mm. test tube.
2. Add 2.5 ml. of 10-percent trichloracetic acid.
3. Place thumb over tube and gently invert twice to mix contents (avoid foaming).
4. Allow to stand 5 to 10 minutes. Again gently invert tube.
5. Pour fluid into photoelectric colorimeter cuvette and determine percent transmission at approximately 420-mu wave length. Any instrument may be used which will accommodate a 5-ml. volume.
6. Convert percent transmission to milligrams percent total protein by reference to a calibration chart. This chart may be prepared by testing several concentrations of a serum of known protein content and plotting the percent transmission values of the turbidities thus obtained on semilogarithmic paper.

In order to investigate the possible effect of changes in albumin-globulin ratio on determined total protein values, fluids were prepared with known protein concentrations, together with varying albumin-globulin ratios.

Albumin and globulin fractions of serum were separated by the method of Pillemer and Hutchinson (*5*). Globulin was precipitated at low temperature, employing methanol and an acetate buffer. Precipitated globulin was redissolved in isotonic saline. Methanol was removed from the albumin solution by dialysis. Protein content of each solution was determined by micro-kjeldahl analysis.

The relatively low protein content of spinal fluid necessitated concentration prior to subsequent separation of the albumin and globulin fractions. Large quantities of pooled spinal fluid were lyophilized and restored to one-tenth original volume with distilled water. Isotonicity was then reestablished by dialysis against distilled water and 0.9-percent salt solution. Separation of albumin and globulin was then accomplished by the addition of saturated ammonium sulfate solution. After removal of the ammonium salt by dialysis, the concentration of stock albumin and globulin solutions were calculated from micro-kjeldahl findings.

Comparative Testing

Solutions of desired protein concentration were prepared from stock globulin and albumin solutions (obtained from serum and spinal fluid) by dilution with 0.9-percent salt solution. Mixtures containing globulin and albumin in the proportions of 1 : 1 and 1 : 4 and solutions of albumin and globulin alone at total protein concentrations of 20 mg. percent and 40 mg. percent were prepared from the stock solutions. Total protein values obtained by testing these solutions with 5-percent sulfosalicylic acid are recorded in table 1.

Table 1.—***The effect of changes in albumin-globulin ratio on the total protein values obtained with 5-percent sulfosalicylic acid on mixtures prepared from serum and spinal fluid fractions***

Mixtures tested		Total protein values	
Parts albumin	Parts globulin	Serum fractions (mg. percent)	Spinal fluid fractions (mg. percent)
		20 mg. percent concentration [1]	
1	0	32	31
4	1	23	23
1	1	17	15
0	1	15	14
		40 mg. percent concentration [1]	
1	0	54	50
4	1	45	43
1	1	35	36
0	1	27	29

[1] These concentrations were prepared by dilution of the stock solutions, the protein content of which was determined by micro-kjeldahl analysis.

It is evident from the results presented in this table that protein values obtained with the Denis-Ayer turbidimetric method are markedly influenced by the albumin-globulin ratio. A solution of albumin, when precipitated with 5-percent sulfosalicylic acid, became more turbid and gave a much higher protein value than did a solution of globulin of like concentration. Mixtures containing 4:1 ratios of albumin to globulin closely reproduced the micro-kjeldahl protein values, but a change in the proportion of the two components to a 1:1 ratio resulted in an apparent change in total protein content, even though the actual protein concentration of the mixture was maintained as a constant.

Table 2.—***Comparative total protein values obtained with 5-percent sulfosalicylic acid and 10-percent trichloracetic acid on mixtures of albumin and globulin prepared from serum***

Mixtures tested		Total protein values	
Parts albumin	Parts globulin	5-percent sulfosalicylic acid (mg. percent)	10-percent trichloracetic acid (mg. percent)
		80 mg. percent concentration [1]	
1	0	90	74
4	1	78	76
1	1	64	74
0	1	50	76
		60 mg. percent concentration [1]	
1	0	78	57
4	1	64	57
1	1	52	57
0	1	40	56
		40 mg. percent concentration [1]	
1	0	54	37
4	1	45	38
1	1	35	37
0	1	27	38
		20 mg. percent concentration [1]	
1	0	32	23
4	1	23	20
1	1	17	19
0	1	15	20
		10 mg. percent concentration [1]	
1	0	17	10
4	1	13	9
1	1	10	10
0	1	9	10

[1] These concentrations were calculated from micro-kjeldahl values obtained on the stock albumin and globulin solutions.

Several protein precipitants were tested in a search for one which would give comparable electrophotometer readings with both albumin and globulin solutions. Of these tested, trichloracetic acid was found to be most satisfactory when equal parts of 10-percent solution were mixed with spinal fluid. Comparative results produced by trichloracetic and sulfosalicylic acid on solutions of albumin and globulin at several total protein concentrations are presented in tables in 2 and 3.

Results produced by the trichloracetic acid procedure were in closer agreement with those of the micro-kjeldahl tests than were the findings by the sulfosalicylic acid method. Values obtained on solutions of the same protein concentration, when tested with sulfosalicylic acid, deviated as much as 40 mg. percent from the micro-kjeldahl value, depending on the amount of albumin or globulin present. The results obtained with trichloracetic

Table 3.—***Comparative total protein values obtained with 5-percent sulfosalicylic acid and 10-percent trichloracetic acid on mixtures of albumin and globulin prepared from spinal fluid***

Mixtures tested		Total protein values	
Parts albumin	Parts globulin	5-percent sulfosalicylic acid (mg. percent)	10-percent trichloracetic acid (mg. percent)
		40 mg. percent concentration [1]	
1	0	54	39
4	1	45	38
1	1	35	39
0	1	27	38
		20 mg. percent concentration [1]	
1	0	31	23
4	1	23	23
1	1	15	23
0	1	14	22

[1] These concentrations were calculated from microkjehldahl values obtained on the stock albumin and globulin solutions.

acid, on the other hand, varied not more than 6 mg. percent from the micro-kjeldahl analysis estimates, regardless of the albumin-globulin ratio.

A limited number of tests were performed on spinal fluids from selected donors, using both sulfosalicylic acid and trichloracetic acid as precipitating agents. In a total of 442 fluids tested, 273 (62 percent) gave the same findings with both methods within the limits of ±5 mg. percent; 141 (32 percent) were higher with the sulfosalicylic acid method; and 28 (6 percent) were lower. No attempt has yet been made to correlate the protein values thus obtained with the clinical findings.

Discussion

The dependability of the micro-kjeldahl procedure for the determination of blood proteins is unquestioned. However, this method is not readily adapted to the routine testing of spinal fluids.

The tyrosine-equivalent method of Johnston and Gibson (*3*) was found to give excellent results in tests on spinal fluids. Determinations were easily reproducible within the limits of ±1.2 mg. percent and correlated closely with values obtained by micro-kjeldahl analysis. As in the case of the micro-kjeldahl, however, the presence of merthiolate (as a spinal fluid preservative) rendered the test unsuitable for use in this laboratory, since concentrations as low as 1:5000 intensified the blue color produced by tyrosine, resulting in abnormally high protein values.

The turbidimetric procedure employing sulfosalicylic acid as a protein precipitant was found to give results which agreed closely with those obtained with the chemical assay methods when tests were performed on fluids containing "normal" albumin-globulin ratios. Changes in this ratio, however, altered the total protein value (as interpreted by sulfosalicylic acid precipitation), despite the fact that the total concentration of the two components was maintained as a constant.

Trichloracetic acid, on the other hand, proved particularly suitable as a precipitant with spinal fluid. Its use as a quantitative protein precipitating agent in chemical procedures is well known, and it readily lends itself to incorporation into a rapid turbidimetric procedure which renders results that reflect true protein concentrations regardless of albumin-globulin ratios.

Lesser amounts of spinal fluid may be tested in the same proportion provided that the electrophotometer employed is adaptable to the use of smaller cuvettes.

Summary

1. Total protein values obtained with the Denis-Ayer turbidimetric procedure employing sulfosalicylic acid compared favorably with values obtained by micro-kjeldahl analysis but only on fluids containing "normal" ratios of albumin and globulin.

2. Changes in albumin-globulin ratio had no detectable effect on total protein values produced by the trichloracetic acid method described.

3. A quantitative turbidimetric procedure for the estimation of total protein content of spinal fluid, employing trichloracetic acid, is described.

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Preservation and Inoculation Studies on *Treponema Pallidum*[1]

Charlotte McLeod, Sc. D., and R. C. Arnold, Senior Surgeon, United States Public Health Service

Introduction

For many years virulent Treponemata could be maintained under laboratory conditions only by continued passage of strains in susceptible animals. As a result of the work of Turner (*1*), it is now possible to preserve the viability and virulence of Treponemata for years, and probably indefinitely, in vitro. This is accomplished by storing the organisms in a freezing cabinet in which a temperature of —78° C. is maintained by means of solid carbon dioxide. However, the difficulty experienced recently in obtaining solid carbon dioxide has led to a further investigation of the effects of storage at —20° C. on the preservation of *Treponema pallidum.* The result of this study is the subject of the present report.

The effect of exposure to a temperature of —20° C. on Treponemata was studied by Turner (*1*) in a limited series of experiments. The organisms were frozen in saline suspensions, and infectivity for rabbits was tested after a storage period of 2 months. Virulence tests with spirochetes frozen at —78° C. and later removed to a temperature of —20° C. were not completed. Organisms frozen at —20° C. and stored at this same temperature failed to survive, while spirochetes initially frozen at —20° C. and then stored at —78° C. produced typical syphilitic lesions in the test animals.

Experimental Methods

Spirochete suspension.—The Nichols strain of *Treponema pallidum* was used in the experiment. A spirochete suspension was prepared aseptically from the testicles of rabbits with early syphilitic orchitis. The testicles were minced, ground in a mortar with sand, and diluted with an amount of 10-percent rabbit serum broth which corresponded to the weight of the tissue in grams. The suspension was centrifuged to sediment the sand and large tissue particles. The resulting supernatant fluid constituted the spirochete suspension, which was then tubed in 1-cc. amounts and frozen. Darkfield examination of the suspension showed the presence of 5 to 10 actively motile spirochetes per oil immersion field. The interval between killing the rabbits and freezing the suspension was less than 2 hours.

Method of freezing.—The tubes containing the spirochete suspension were divided into four groups and treated in the following manner:

(1) Frozen at —20° C., stored at —20° C.
(2) Frozen at —20° C., stored at —78° C.
(3) Frozen at —78° C., stored at —78° C.
(4) Frozen at —78° C., stored at —20° C.

Freezing and storage at —78° C. were carried out in a freezing cabinet cooled with solid carbon dioxide (*2*). Freezing and storage at —20° C. were effected in an electrically operated refrigerator. For freezing at these temperatures, the tubes were immersed in 95-percent alcohol which had been previously brought to the desired temperature in the —20° C. or —78° C. freezing unit. The tubes were left at the respective freezing temperatures for a period of 2 hours and were then removed from the alcohol for storage at the respective maintenance temperatures.

Method of testing.—Tests for viability and virulence of the spirochetes were made by inoculation of rabbits with a test dose of 0.3 cc. of the suspension. The virulence of the fresh, unfrozen suspension was established by inoculating two rabbits in the right testicle. The frozen material, after rapid thawing in a water bath at 37° C. and subsequent darkfield examination, was tested by inoculation of the test dose both in the right testicle and in the scrotal skin of the left testicle of the same rabbit. The spirochetes stored at −20° C. (initially frozen at −20° C. or at −78° C.) were tested 3 weeks, 8 weeks, and 16 weeks after freezing. Five rabbits were used for each sample tested at each time interval. The organisms stored at −78° C. (initially frozen at −78° C. or at −20° C.) were tested 1 year after freezing. Two rabbits were used for each sample tested. The animals were examined twice weekly after inoculation, and specificity of lesions was determined immediately upon their appearance by darkfield examination of fluid aspirated from the testicle or scrotal skin. Lymph node transfer from each rabbit which failed to develop lesions was carried out by implanting the inguinal and popliteal nodes in the scrotal sac of a normal animal. All test rabbits were observed for a period of 90 days.

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[1] From the Venereal Disease Research Laboratory, U. S. Marine Hospital, Staten Island 4, N. Y. Medical Director J. F. Mahoney in charge.

Experimental Results

The two rabbits inoculated intratesticularly with the fresh, unfrozen spirochete suspension developed syphilitic lesions in 21 days.

The organisms in the sample of spirochete suspension stored at −78° C. for a period of 1 year (initially frozen at −78° C. or at −20° C.) were actively motile when thawed and produced lesions of both the right testicle and the left scrotum in the four rabbits inoculated. The longest period of incubation of the lesions was 35 days. These results are illustrated in table 1.

The results of rabbit inoculations with Treponemata stored at −20° C. are shown in table 2. Spirochetes initially frozen at −78° C. failed to survive as long as organisms initially frozen at −20° C. The spirochetes frozen at −78° C. produced lesions in three of the five test rabbits inoculated at the end of the 3-week storage period, in two of the four surviving rabbits inoculated at 8 weeks, and in none of the four surviving rabbits inoculated at 16 weeks. On the other hand, the organisms which were both frozen and stored at −20° C. produced lesions in all the five rabbits inoculated at the end of the 8-week storage period and in three of the five rabbits inoculated at 16 weeks. Lymph node transfers from all rabbits which failed to develop lesions were negative. A very occasional feebly motile spirochete was found in each sample of suspension which was thawed up to the end of the 8-week storage period. After longer storage, no motile organisims were seen.

Of the 13 rabbits which showed evidence of syphilitic infection as a result of inoculation with spirochetes stored at −20° C., all developed scrotal chancres, while only 5 developed testicular lesions. The incubation period of the lesions varied from 38 to 66 days. As the stor-

Table 1.—*Results of rabbit inoculations with* Treponema pallidum *after storage for 1 year at −78° C.*

Spirochetes frozen at −78° C., stored at −78° C.					Spirochetes frozen at −20° C., stored at −78° C.				
Rabbit No.	Inoculated in testicle		Inoculated in scrotal skin		Rabbit No.	Inoculated in testicle		Inoculated in scrotal skin	
	Lesion	Incubation period (days)	Lesion	Incubation period (days)		Lesion	Incubation period (days)	Lesion	Incubation period (days)
389	Positive	30	Positive	33	387	Positive	33	Positive	33
390	do	35	do	35	388	do	35	do	35

Table 2.—*Results of rabbit inoculations with* Treponema pallidum *after storage at —20° C.*

Storage period (weeks)	Spirochetes frozen at −78° C., stored at −20° C.					Spirochetes frozen at −20° C., stored at −20° C.				
	Rabbit No.	Inoculated in testicle		Inoculated in scrotal skin		Rabbit No.	Inoculated in testicle		Inoculated in scrotal skin	
		Lesion	Incubation period (days)	Lesion	Incubation period (days)		Lesion	Incubation period (days)	Lesion	Incubation period (days)
3	207	Positive	42	Positive	42	--------	--------	--------	--------	--------
3	208	Negative	--------	do	42	--------	--------	--------	--------	--------
3	209	do	--------	Negative	--------	--------	--------	--------	--------	--------
3	210	do	--------	Postive	56	--------	--------	--------	--------	--------
3	211	do	--------	Negative	--------	--------	--------	--------	--------	--------
8	217	do	--------	do	--------	222	Positive	38	Positive	38
8	218	do	--------	Positive	66	223	do	45	do	45
8	219	Died 21 days.	--------	--------	--------	224	do	68	do	68
8	220	Negative	--------	Positive	66	225	Negative	--------	do	42
8	221	do	--------	Negative	--------	226	Positive	38	do	38
16	293	Died 21 days.	--------	--------	--------	298	Negative	--------	Negative	--------
16	294	Negative	--------	Negative	--------	299	do	--------	Positive	54
16	295	do	--------	do	--------	300	do	--------	Negative	--------
16	296	do	--------	do	--------	301	do	--------	Positive	60
16	297	do	--------	do	--------	302	do	--------	do	54

age period of the spirochetes was prolonged, the incubation period of the lesions tended to lengthen, and fewer testicular lesions were produced.

Discussion

Experimental work relating to the effects of freezing and thawing upon the viability of cells and theories regarding the mechanisms by which cells are adversely affected by these processes have been reviewed by Turner (*1*). In the present experiment, suspensions of *Treponema pallidum* in 10-percent rabbit serum broth, which were maintained at a temperature of —20° C., were infective for rabbits after a storage period of 4 months. Spirochetes which were stored at —78° C., after freezing at this temperature or at —20° C., remained viable for a period of 1 year. These observations support the conclusions of Turner (*1*) that Treponemata are damaged during storage at —20° C., but not during the freezing process at this temperature.

Spirochetes survived for a longer period during storage at —20° C. if they were initially frozen at —20° C., rather than at the lower temperature of —78° C. From these results it is apparent that exposure to a continuous storage temperature of —20° C. is less harmful to the spirochete than a gradual change of temperature from —78° C. to —20° C. The adverse effect of slow warming or thawing on the viability of spirochetes has been demonstrated also by Turner and Brayton (*3*) using the organisms of relapsing fever.

Rabbits infected with spirochetes stored at —20° C., as a result of inoculating the test dose in both the right testicle and the left scrotum, developed a larger number of scrotal lesions than of testicular lesions. The appearance of scrotal lesions in the absence of testicular lesions occurred more frequently as the period of storage lengthened and, presumably, as the number of viable organisms in the inoculating dose decreased. It would seem from these results that the scrotal skin of the rabbit is a more favorable site than the body of the testicle for the survival of *Treponema pallidum*. This subject is now under further study.

Summary

1. Suspensions of *Treponema pallidum* stored at —78° C., after freezing at —78°

C. or at —20° C., were viable after a storage period of 1 year.

2. Spirochetes stored at —20° C. remained viable for a period of 4 months. Survival was longer at this temperature if the initial freezing was carried out at —20° C., rather than at —78° C.

3. Rabbits inoculated with the frozen spirochetes developed lesions more frequently as a result of intradermal inoculation of the scrotum than as a result of intratesticular inoculation.

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Out-Patient Attendance of Early Syphilis Patients Treated by Private Physicians in Vermont

R. B. Aiken, M. D., Secretary and Executive Officer, Vermont Department of Public Health

In October 1946, the Vermont Department of Public Health undertook an experiment to explore the feasibility of out-patient treatment of syphilis by private physicians. The State furnished the physicians with penicillin in peanut oil-beeswax with the recommendation that patients with early syphilis be treated with 600,000 units per day for 8 successive days to a total of 4,800,000 units. The physicians were asked to report the attendance record of each patient to the State Department of Public Health. An analysis of the first 101 cases was published in the October 1947 issue of THE JOURNAL OF VENERAL DISEASE INFORMATION.[1]

Presented herewith is a summary of the attendance records of cases reported during the life of the project, which ended July 1, 1948. A total of 193 patients, reported by 84 doctors, started treatment on the recommended schedule. Of these, 140 (72.5 percent) kept all appointments; 49 (25.4 percent) missed one or more appointments, but completed treatment; while only 4 (2.1 percent) did not complete treatment. Thus, from the standpoint of the completion of prescribed treatment by 97.9 percent of the patients, the experiment may be said to have successfully demonstrated the ability of Vermont doctors to hold patients to a daily schedule of treatment. These patients, who were white and about evenly distributed as to sex, were predominantly (75 percent) primary and secondary syphilis cases.

Table 1 shows in partial detail the regularity of attendance of those patients beginning the recommended regimen. For comparative purposes, the data are given separately for each year of the life of the project, the figures for 1947 being essentially the same as those published earlier. The increase in the percentage of patients requiring prolonged treatment (17.8 percent in 1947 and 31.2 percent in

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[1] "Attendance Record of Patients Treated by Private Physicians," by R. B. Aiken, pp. 224–225.

Table 1.—*Regularity of attendance of patients treated on an out-patient basis—4,800,000 units of penicillin in peanut oil-beeswax (600,000 units daily for 8 days)*

	Total		1947		1948	
	Number	Percent	Number	Percent	Number	Percent
Total cases treated	193	100.0	84	100.0	109	100.0
Completed treatment in 8 consecutive days	140	72.5	68	81.0	72	66.0
Lapsed without completing treatment	4	2.1	1	1.2	3	2.8
Treatment required from 9 to 15 days	49	25.4	15	17.8	34	31.2

1948) was caused largely by the failure of a greater number of doctors to give treatment on Sunday.

Table 2 presents a break-down of the reasons in the 49 cases, which received prolonged treatment in both years, insofar as those reasons were stated. Of the 27 cases listed under unavailability of doctor, only 3 were recorded as such; the remaining 24 showed that treatment was given for 8 days within inclusive dates which covered 9 calendar days. It was assumed therefrom that the doctor did not administer treatment on Sunday. Treatment reactions caused five interruptions; one patient had a reported temperature of 107° F.; two had severe local soreness; and two were generally ill.

Thirty-one patients on other schedules received penicillin in various intervals, doses, and total amounts, but all received a complete schedule of treatment.

Table 2.—*Patients receiving interrupted but complete treatment, by reason for prolongation of treatment period*

	Number
Total patients	49
Doctor unavailable	27
Treatment reaction	5
Transportation	2
Misunderstanding	2
Accident or illness in family	2
No reason given	11

CURRENT LITERATURE

NOTE: Abstracts of any article listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

ACTA CHIR. SCANDINAV., STOCKHOLM

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ACTA DERMAT.-VENEREOL., STOCKHOLM

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AM. J. DIS. CHILD., CHICAGO

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AM. J. M. SC., PHILADELPHIA

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*Unknowns in the biology of syphilitic infection. Paul D. Rosahn. Symposium on Syphilis. 5 : 631–640, Nov. 1948.

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*Nationwide results in the treatment of early syphilis with penicillin. Frank W. Reynolds. Symposium on Syphilis. 5 : 679–686, Nov. 1948.

*Penicillin treatment of early syphilis. Evan W. Thomas. Symposium on Syphilis. 5 : 687–692, Nov. 1948.

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Unknowns in the biology of syphilitic infection. Paul D. Rosahn. Symposium on Syphilis. Am. J. Med., New York, 5 : 631–640, 1948.

The purpose of this article is to discuss those areas in the biology of syphilis which merit further exploration. There is one dominating mystery, and that is why it has not been possible to grow the specific etiologic agent in its pathogenic form on artificial culture media. Propagation of viruses is possible only in the presence of the living cell. Closely related to the problem of the growth requirements of the treponeme is its inadequately understood chemical constitution.

Syphilis can be successfully transferred to mice and rabbits, but the cause of the different reactions is still unknown. There are peculiar qualities in the mouse which prevent organisms below the minimal infectious number from obtaining a foothold in the tissues where they may multiply until they reach the level of infectivity for the rabbit. If it were known whether or not there are treponeme inhibitory factors operative in the mouse, and if so, could they be identified and isolated, the information might be of practical value when applied to the prevention of the disease in man. A knowledge of the fundamental biologic differences among mice, rabbits, and humans which are responsible for their differing reactions to syphilitic infection would enhance the understanding of the disease. The disease in rabbits more nearly approaches the manifestations of human syphilis, yet there are factors operative in rabbit skin that inhibit the skin manifestations which occur in humans. Syphilitic lesions of the cardiovascular or central nervous systems have never been observed in rabbits, but so far as is known large groups of syphilitic rabbits have never been held for their entire life span with autopsies at death to determine the presence or absence of involvement of the nervous and circulatory systems. Such an experiment might throw light on the problem of tissue localization of syphilitic lesions.

There are innumerable unsolved laboratory and clinical problems in human syphilis. There is little known about natural or specific immunity to syphilis. The influences that operate to localize the infection in vital organs in some persons, or to inhibit the development of specific lesions in others are unknown.

There is need for further study on false positive reactions and of the time and method of fetal infection in congenital syphilis. There is need for clearer differentiation between reinfection and relapse. Modern technics in physical and chemical research can well be adapted to elucidating many of the mysteries in the life history of syphilitic infection.

Nationwide results in the treatment of early syphilis with penicillin. Frank W. Reynolds. Symposium on Syphilis. Am. J. Med., 5 : 679–686, 1948.

The conclusions attained in this report were based upon the results of two Nation-wide studies on the penicillin treatment of early syphilis. One study was begun under the auspices of the Committee on Medical Research and continued by the Syphilis Study Section, National Institutes of Health, and the other was under the direction of the Venereal Disease Division, United States Public Health Service, through its rapid treatment centers. As defined in previous reports, the ideal treatment for syphilis is one that is completely and uniformly effective, entirely devoid of toxicity, and readily administered with a minimum of inconvenience to the patient and the physician.

As for efficacy, penicillin alone is somewhat inferior in the therapeutic activity to properly administered metal chemotherapy, provided the latter is carried out completely. Recurrent infectious lesions continue to be reported after penicillin therapy. Crystalline penicillin G is superior to amorphous penicillin especially when the latter contains a significant content of penicillin K. Therapeutic results with penicillin-oil-beeswax (POB) have been perhaps slightly better than those with comparable amounts of penicillin in aqueous solution. The results of penicillin therapy are influenced by the compositions of the patient population, which accounts for the discrepancies in various studies.

The fact that penicillin has caused no reported fatalities and comparatively few serious reactions continues to be one of the most remarkable attributes of the drug.

As for ease of administration, penicillin is superior to other forms of therapy. An ambulatory preparation, penicillin in oil with 4.8 percent beeswax, was evaluated in both the Nation-wide studies and found to be as efficacious as comparable amounts of penicillin in aqueous solution. Superior to POB is procaine penicillin which causes no painful local reactions thus making the course of therapy more tolerable to the patient.

Although penicillin falls short of being the ideal form of therapy, largely on the basis of its limitations in therapeutic efficacy, there are possibilities of altering the time-dose relationships to increase blood and tissue concentrations, and administering other spirocheticides concomitantly with penicillin.

Penicillin treatment of early syphilis. Evan W. Thomas. Symposium on Syphilis. Am. J. Med., 5: 687–692, 1948.

The data on the results of the treatment of early syphilis with penicillin are limited to the use of aqueous solutions and penicillin in oil and beeswax. From information now available, penicillin must be active within the body for 2 to 4 days to cure many cases of early syphilis, and the optimum period of treatment seems to be at least 15 days.

It has been shown that when injections of aqueous solutions of penicillin were given every 2 to 4 hours in an 8-day period of therapy, a total dose of 2.4 million units gave as good results as when 5 million units were given in the same period. The failure rates for the 8-day schedules with at least 2.4 million units of penicillin have been about 20 percent.

When penicillin-oil-beeswax is used, daily injections of 300,000 to 600,000 units are advised for 15 days. Data on the 15-day schedules are less adequate than on the 8-day schedules, but the 15-day treatment seems to have given better results than the 8-day.

Procaine penicillin G in oil gelled with 2-percent aluminum monostearate promises to simplify the treatment of early syphilis. It now seems probable that an injection of 1.2 million units of this preparation once a week for 2 weeks, or 2 injections of 600,000 units twice a week for 3 weeks will give the same penicillin action as daily injections of 300,000 units of penicillin-oil-beeswax for 15 days.

Patients given rapid treatment for early syphilis must be observed at frequent intervals for at least 2 years with quantitative serologic tests. About 75 percent of successfully treated patients become seronegative within 6 months after treatment. The other 25 percent may have low reagin titers for varying periods after 6 months, but they do not require re-treatment unless the titers show evidence of relapse or reinfection. Of the probable relapses observed at Bellevue Hospital, over 80 percent occurred between the third and twelfth months after treatment.

The evaluation of rapid treatment of early syphilis would be much more exact if it were possible to differentiate between relapses and reinfections in all cases.

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La paralysie générale et le tabès chez l'indigène congolais. (General paralysis and tabes amongst the Africans of the Congo.) P. Limbos. 27 : 373–380, Dec. 31, 1947. [Abstracted in Bull. Hyg., London, 23 : 772–773, Oct. 1948.]

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*Penicillin in treatment of neurosyphilis. IV. Tabes dorsalis. L. Parker Chesney and Frank W. Reynolds. 59 : 347–359, Mar. 1948.

Clinical aspects of cerebral cysticercosis. [Syphilis.] S. Obrador. 59 : 457–468, Apr. 1948.

Penicillin in treatment of neurosyphilis. IV. Tabes dorsalis. L. Parker Chesney and Frank W. Reynolds. Arch. Neurol. & Psychiat., 59 : 347–359, 1948.

In connection with the Nation-wide evaluation of penicillin in the treatment of syphilis, the authors report their results with the use of this drug in treating tabes dorsalis, a study which has been in progress at Johns Hopkins Hospital since October 1943.

As of October 1946, 54 patients with tabes dorsalis have received penicillin therapy. Thirty-three of these patients received penicillin alone in amounts ranging from 1,200,000 to 20,000,000 units in divided doses. The remaining 21 patients received from 1,800,000 to 20,000,000 units of penicillin in divided doses concurrently with induction of malarial fever. Data are provided on the age, race, and sex distributions, the duration of symptoms, the extent of pretreatment abnormalities of the cerebrospinal fluid, the duration of posttreatment observation, and the effects of therapy.

Although the number of patients treated is small and the period of posttreatment observation far too brief to permit definitive, statistically valid conclusions, the authors make some comparisons between the two methods of therapy. From the standpoint of symptomatic improvement, the results are strikingly better after combined malarial and penicillin therapy than after penicillin therapy alone. With penicillin therapy alone, preliminary results indicate that in 27 percent of the patients the symptoms were significantly improved, whereas in 57 percent of patients treated with malarial and penicillin therapy there was significant symptomatic improvement. The response in the abnormalities of the cerebrospinal fluid is also more satisfactory after the combined therapy, although here the difference is less striking. In the group receiving combined therapy, febrile Herxheimer reactions could not be detected in any of the patients, since penicillin was given concurrently with the malarial treatment. In the group receiving penicillin alone, febrile Herxheimer reactions occurred only in patients with spinal fluids which gave strongly positive reactions for syphilis and were far less frequent than among patients with dementia paralytica.

With penicillin therapy alone, the best clinical results were noted in patients in whom the manifestations of tabes were of comparatively recent onset, in whom there were evidences of "activity" in the spinal fluid prior to therapy, and in whom the response of the cerebrospinal fluid was promptly favorable. With combined malarial and penicillin therapy, favorable clinical responses were obtained nearly as often in patients whose symptoms were of long standing as in those whose symptoms were of recent appearance.

In conclusion, the authors state that evidence indicates that penicillin therapy alone is somewhat inferior to therapy of the prepenicillin era, except in respect to its convenience and relative lack of toxicity, but currently administered penicillin and therapeutic malaria is the most effective form of therapy now available for tabes dorsalis.

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CURRENT NOTES AND REPORTS

Educational Program at Alto Medical Center—Alto, Georgia

Dorothy Johnston, Assistant Nurse Officer (R) United States Public Health Service

In January 1947, a public health nurse was placed in the Alto Medical Center, Alto, Georgia, to conduct an educational program and to perform related liaison work with community agencies.

After making definite determination as to objectives, a careful analysis was made of the background of the patients to be treated and of the facilities at hand to work with. The objectives were fourfold: (1) to instruct venereal disease patients regarding the nature of their disease, the means of prevention, the necessity of completing scheduled treatments, and the importance of reporting all contacts; (2) to develop a broad health program; (3) to conduct in-service training and orientation programs for members of the hospital staff; and (4) to coordinate and integrate the health program of the rapid treatment center with that of the community.

Alto Medical Center is equipped to accommodate 750 patients. These patients come from both rural and urban areas; they represent every type of employment; educationally, they range from the illiterate to the well-educated, and economically, from public welfare cases to patients with an annual income of $8,000 or more.

Their problems were as varied as their backgrounds, and for that reason it seemed advisable to give as much individual instruction as time allowed. Obviously, the best way to give this instruction was by personal interview. It should be said in this connection that the hospital staff of trained personnel gave liberally of their time and energy to study the problems of individual patients so that they could fit the instruction to meet the needs of the individual. It was fortunate also, that the hospital had sufficient space to permit the staff to conduct these interviews in pleasant surroundings in complete privacy.

Since a large number of the patients could not read, it was necessary to place considerable emphasis on visual and auditory aids. A variety of posters showing venereal disease lesions were obtained and placed on bulletin boards for display in the wards and day rooms. These posters were flanked by flash cards identifying the disease, not only by the proper name but by various names commonly associated with it, and explaining the various stages of the disease. Periodically these posters were replaced by other types of posters relating to other communicable diseases and to other phases of the health program, such as nutrition and infant and maternity care.

In addition to the posters, a series of eight wall placques were designed by artists from the State health department. These placques, made in distinct and separate colors, identified the various stages of syphilis and were correlated to the patient's treatment card in such a way that a patient having primary syphilis and using a yellow card would be especially interested in the yellow placque describing primary syphilis.

Moving pictures were shown once a week to men and women, white and nonwhite, but in separate groups. Films such as are provided in the Columbia University series were used and, in addition, several films were borrowed from the Navy. At the conclusion of each picture, one of the staff physicians gave an informal talk and answered questions which the patients had previously written out and placed, unsigned, in boxes especially constructed for this purpose and placed in convenient locations throughout the building. Patients were also encouraged to ask questions from the floor.

Another medium of group instruction which had wide appeal was the transcription. Facilities at the Alto Medical Center are especially adequate for this medium since it has a centrally controlled sound system with speakers placed in all wards and even outside of the building. Various recordings were used with success—"The Torchy Series" from the United States Public Health Service, "Help yourself to Health Services" from the United States Office of Education and, most important of all, recordings made by the Center itself.

On a semiprofessional recording device, which belongs to the Center, transcriptions were made in true "Quiz Kid" style—programs in which members of the staff acted as masters of ceremony, and the patients answered the questions. Patients who participated in these programs had had some venereal disease instruction prior to the program but they did not know in advance what questions would be asked. Simple prizes were awarded for correct answers. Eager response to this type of program emphasized again the value of projects in which the patients themselves participate.

Another service especially designed for the patients was a weekly newspaper which carried news of special interest to patients, and featured at least one article on some phase of health. Patients looked forward to receiving this paper and often asked to be allowed to take a copy home as a souvenir.

Liberal use was made, of course, of venereal disease informational material written for the lay public. Literature of this kind, together with information on other health publications, was placed on each floor in racks especially prepared for this purpose by the hospital maintenance staff.

This, in brief, describes the health program within Alto Medical Center. However, the real problems of public health cannot be solved entirely within a hospital. Economic insecurity, bad working conditions, broken homes, lack of appropriate educational and recreational facilities form a large part of the whole picture surrounding the individual and his illness. In all the interviews conducted, an attempt was made to look beyond the immediate illness of the patient and to study the environment from which he came for the purpose of determining what conditions in his home or in his community might interfere with the maintenance of positive health. Then, in so far as possible, unfavorable conditions were brought to the attention of appropriate authorities for correction, or, in many instances, the patient was advised as to what community services were available to him which might help him with his immediate problems. The nurse thus serves in a liaison capacity between the rapid treatment center and the State and local health agencies, voluntary welfare groups, private physicians, civic organizations, labor and management groups, and leaders in church and school, in their combined effort to mobilize all constructive forces to improve living conditions for all citizens, especially for the underprivileged.

Public Health Nursing Fellowships

Two 6-month fellowships in venereal disease nursing, running consecutively and giving each fellow a $1,500 stipend, are being offered annually by the Institute for the Study of Venereal Disease, University of Pennsylvania, Philadelphia 4, Pa. Fellows are expected, however, to pay their own tuition.

The purpose of these fellowships is to prepare nurses to become venereal disease nursing consultants on local and State levels. In order to be eligible for consideration, applicants must: (1) be graduates of an accredited school of nursing; (2) have a B. S. degree with a major in (*a*) public health nursing, (*b*) social case work, or (*c*) nursing education; and (3) have a minimum of 3 years' postgraduate experience in nursing, including at least one year's experience in public health nursing and one year's experience in a supervisory capacity. Some work in venereal disease control is desirable. In addition, the applicant should have the recommendation of the State health department and a reasonable assurance of an assignment in public health nursing on completion of the course.

The course consists of:

1. P515 and P116 Program in Applied Venereal Disease Epidemiology — 12 weeks, five and three semester credits, respectively.
2. Added selective field experience in venereal disease nursing—4 weeks.
3. Clinic treatment room experience in venereal disease clinic—4 weeks.
4. Course 525 in Health and Human Relations—5 weeks, five semester credits.

Any additional courses in administration, supervision, guidance, and counseling available at the University of Pennsylvania may be taken concurrently with courses P515 and P116.

Nurses interested in being considered for these fellowships should write to Jane Barbara Taylor, R. N., Director of Field Work, Institute for the Study of Venereal Disease, Hospital of University of Pennsylvania, 36th and Spruce Streets, Philadelphia 4, Pa., for additional information and application forms.

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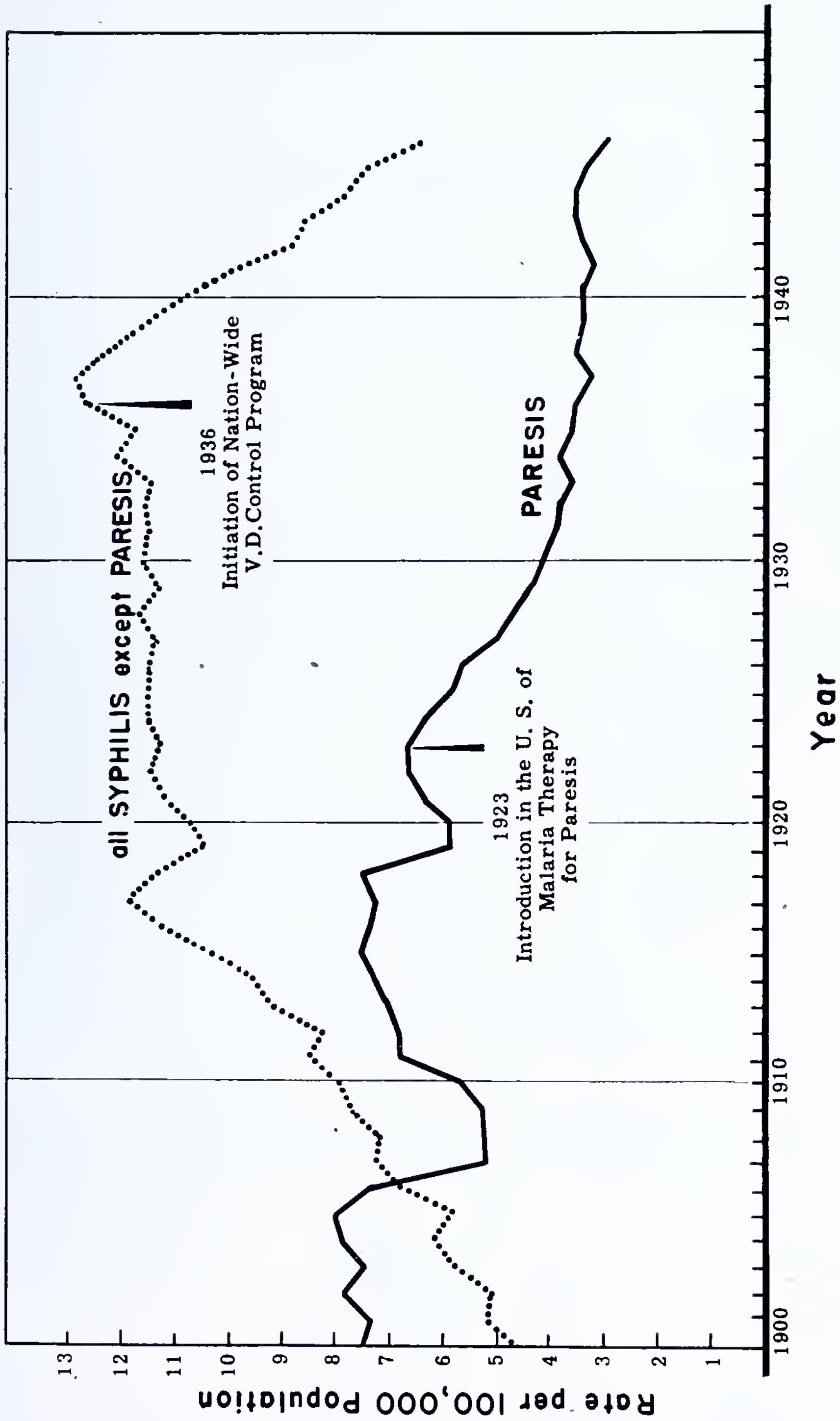

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The JOURNAL of VENEREAL DISEASE INFORMATION

Volume 30 May 1949 Number 5

ORIGINAL ARTICLES

Penicillin Therapy of Early Syphilis: IV 125
R. C. Arnold, *Senior Surgeon*; F. P. Nicholson, M. D.; J. F. Mahoney, *Medical Director*; R. D. Wright, *Surgeon*

Venereal Disease Case Finding in Quitman County, Mississippi . . 127
A. L. Gray, M. D.
Howard Boone, *Health Program Representative*
Richard S. Hibbets, *Health Program Representative*

Socioeconomic Factors in Syphilis, Savannah, Georgia 131
C. D. Bowdoin, M. D., M. P. H.; Quentin R. Remein, *Health Program Analyst*; Clair A. Henderson, M. D.; John W. Morse, *Biostatistician*
Warren T. Davis, Jr., *Health Program Representative*

Contact Investigation of Syphilis 140
Joseph S. Spoto, *Senior Surgeon*
Albert P. Iskrant, *Principal Statistician*

Sugar Fermentations of Gram-Negative Diplococci Isolated From the Genitourinary Tract of Penicillin-Treated Gonorrhea Patients . . 145
Louis Wax, Bacteriologist

CURRENT LITERATURE 147

CURRENT NOTES AND REPORTS

The Prevalence of Syphilis in Pregnant Women in Athens, Greece, From 1935 to 1940 155
D. A. Messinezy, M. D., M. P. H.

STATISTICS

Syphilis and Gonorrhea Reported, Second Quarter Fiscal 1949 . . . 156

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Penicillin Therapy of Early Syphilis: IV[1]

R. C. Arnold, Senior Surgeon;[2] J. F. Mahoney, Medical Director;[2] F. P. Nicholson, Senior Assistant Surgeon;[2] and R. D. Wright, Surgeon[2]

The demonstration of the efficacy of penicillin therapy in early syphilis has proceeded in this clinic in a slow but successful order of events. Investigations were designed to prove that penicillin would cure syphilis and that adjuvant therapy was not necessary. Concomitant observations to determine the optimal duration of aqueous penicillin therapy were carried on. The present problems are concerned with the development and utilization of slowly absorbed penicillin salts and repository vehicles to show that a single-injection therapy will suffice for early syphilis.

That penicillin apparently would cure syphilis was first reported 5 years ago (*1*). The four patients listed in that report have had continued clinical and laboratory studies. The results of these studies now indicate that the original patients were cured. That penicillin can cure early syphilis in man and animals was further confirmed by subsequent reports (*2, 3*). Review of these later schedules definitely demonstrates that in the penicillin therapy of early syphilis supplementary heavy metal therapy is not needed and that the larger doses of aqueous penicillin, administered every 2 hours, give the best results.

Effective dosages having been established, attention was focused on the problem of developing a therapy of less than 7 or 8 days' duration. It was demonstrated that early syphilis in animals could be cured with aqueous penicillin administered for 12, 18, 24, and 48 hours, respectively. Many (but not all) of the syphilitic animals were cured with 12 to 24 hours of continuous therapy. However, maximum effectiveness was obtained after 72 hours. In other words, the cure rate in animals rose sharply when adequate blood levels of penicillin were maintained for 72 hours.

Observations of a similar pattern were noted in the clinical studies reported by the Chicago Intensive Treatment Center (*4*), where it was found that syphilis could be cured in somewhat more than half the patients treated with only 24 hours of aqueous penicillin therapy. But the failure rate prohibited the use of that therapy.

It was significant that even a small percentage of syphilis in man could be cured with only 1 day of penicillin therapy. And it was reasonable to assume that the optimal duration of treatment of early syphilis in man (i. e., curative penicillin concentrations in the body) would be less than 8 days but more than 1 day.

On the basis of this assumption, and as a result of animal experiments, a 3-day therapy was established for clinical trial. This therapy consisted of the intramuscular administration of 200,000 units of aqueous penicillin every 2 hours for 36 injections; total dosage of penicillin 7.2 million units; duration of therapy, 72 hours.

Since the purpose of the study was to determine the cure rate for 3 days of therapy, it was necessary to eliminate the dosage factor from the time-dose relationship. This was effected by fixing the individual dose at 200,000 units, an amount probably far in excess of the optimal dosage. Hence, it was felt that treatment failures would be due to shorter time rather than to size of dose. Optimal dosage could be readily determined, once the time factor was established.

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[1] From the Venereal Disease Research Laboratory and the U. S. Marine Hospital, Staten Island 4, N. Y.

[2] U. S. Public Health Service.

Patients with primary or secondary syphilis were carefully selected according to the following criteria: All patients were darkfield positive (those diagnosed as secondary were darkfield positive from secondary lesions); no patient had a history of previous syphilis; and no patient had received antisyphilitic or penicillin therapy for any condition within the 4 or 5 months preceding his antisyphilitic therapy at this clinic. Post-treatment clinical and serologic examinations were conducted on lines parallel to examinations given patients treated with 40,000 units of aqueous penicillin administered every 2 hours for 85 injections.

Since the criteria for diagnosis and follow-up were the same, it was believed that the results of both schedules might be evaluated on a comparative basis. A comparison of the re-treatment rates for these two schedules at various time periods indicates that the approximate cumulative rate is 5 percent for each. However, the true therapeutic response is not apparent in the cumulative re-treatment rate because both reinfections and relapses are combined to determine this rate. Should the same formula continue to be used for all future reports, the cumulative re-treatment rate would continue to rise each year as reinfections occur.

Treatment failures, i. e., serologic relapse or serologic and clinical relapse, were observed frequently in the early penicillin schedules which utilized 20,000 or 40,000 units of penicillin on a 3-hour basis. These failures were believed to be due principally to a faulty time-dose relationship. With better adjusted schedules, the number of true relapses diminished to a negligible figure.

It was realized, however, that an occasional patient may excrete penicillin very rapidly or may change it to an inactive metabolite. To determine rapidity of penicillin excretion and maintenance of serum concentration levels of penicillin, variations were made in individual dosages and in intervals between injections. These studies indicated that 40,000 units of aqueous penicillin sodium given intramuscularly every 2 hours maintain at least 0.015 units per cubic centimeter in 99.0 percent of patients. If the dosages are increased, the levels are higher, whereas, if lower dosages are used, the maximum sustained serum levels vary a great deal and may account for the increased failure rates of certain penicillin schedules.

It is not expected that the experimental schedules utilizing 200,000 units of aqueous penicillin every 2 hours for 36 injections will be generally adopted for the treatment of early syphilis, since penicillin is wasted by this excessively large dosage. In addition, while this schedule does reduce the period of treatment, it still entails hospitalization of the patient for 3 days. However, the significant point which has been demonstrated by this study is: early syphilis can be cured with only 3 days of adequate penicillin serum concentration. This time factor will probably become the basis for the ambulatory management of syphilis, an eventuality which is dependent upon the utilization of the slowly absorbed penicillin salts and repository vehicles.

When procaine penicillin (300,000 units) incorporated in a 2-percent aluminum monostearate compound was used, serum levels of 0.0125 unit per cubic centimeter were observed for at least 3 days in 95 percent of patients. As a result of these studies, two schedules for the ambulatory treatment of early syphilis have been instituted. In one schedule one injection of 600,000 units of procaine penicillin with aluminum monostearate is given daily for 3 days. In the other a single injection of 300,000 units is given. If it can be demonstrated that a single injection of the slowly absorbed penicillin salt in a repository vehicle is sufficient for the therapy of early syphilis, minimum therapeutic dosage can be established later.

In summary: The favorable clinical and serologic response of early syphilis to 3 days of penicillin therapy may be the key to the solution of the time factor in the ambulatory management of syphilis.

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Venereal Disease Case Finding in Quitman County, Mississippi

A. L. Gray, M. D.;[1] Howard Boone, Health Program Representative, and Richard S. Hibbets, Health Program Representative, United States Public Health Service

On September 1, 1947, the Quitman County Health Department, with the cooperation of the Mississippi State Board of Health and the United States Public Health Service, put into operation a venereal disease case-finding project to demonstrate the effectiveness of a well-balanced program of intensive venereal disease education, vigorous contact investigation, and screen testing.

Quitman County is in a fertile, sparsely populated, agricultural region in the northwestern part of Mississippi. In 1947, its 395 square miles were estimated to contain only about 28,560[2] persons, of whom 65 percent were nonwhite. The only town of any size is Marks, the county seat (approximately 2,000 persons). At the time the project opened in September 1947, the health services in the county were inadequate, since the health department was staffed by only a part-time health officer, a nurse, a clerk, and a part-time venereal disease investigator.

The project organization consisted of seven persons: a project director (nurse), a clinician (doctor), a clinician's assistant (nurse), a clerk, and three venereal disease investigator-educators. The project director, who was administratively responsible for project operation to the Director of the Division of Preventable Disease Control of the Mississippi State Board of Health, was selected because of her extensive nursing and administrative experience and her ability to achieve harmonious relationships between county health departments, civic organizations, business and professional groups, and the people of the community.

Eight venereal disease diagnostic clinics, each providing complete facilities for the clinical diagnosis of venereal disease and for the treatment of gonorrhea, were established in convenient locations so that no individual had to travel more than 6 miles to obtain diagnostic service, which was available to both white and nonwhite persons. The twelve 3-hour clinic meetings which were held each week in these eight clinics were arranged so that two investigators could be working in the field while the third attended the clinic in operation at the time. All persons suspected of having venereal disease (other than gonorrhea) were referred either to the Delta Medical Center at Greenwood, Miss., or to a local private physician for final diagnosis and/or treatment.

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[1] Director of Preventable Disease Control, Mississippi State Board of Health.

[2] Annual Bulletin of Vital Statistics, 1947, vol. 1, State Summary. Published by the Mississippi State Board of Health.

Case-Finding Methods

Venereal Disease Education and Publicity

Approximately 30 days prior to the beginning of the project, a meeting conducted by representatives of the Mississippi State Board of Health and the United States Public Health Service and attended by city officials, owners, and managers of the larger plantations, and other health-minded citizens was held in the courthouse in Marks (the county seat) for the purpose of enlisting the aid of key individuals and informing community leaders of the details of the project. A report of the proceedings of this meeting and follow-up articles periodically reporting on the progress and results attained in the project were published in the Quitman County newspaper and in other newspapers having a large circulation in the county. These articles did much to maintain a high interest level throughout the 10 months of the project period.

A constant flow of venereal disease educational material was channeled through the mail to plantation owners and operators, school teachers, and church and civic leaders, special material being sent on holidays. For example, in the special New Year bulletin, the people were urged to "start the year off right" by helping to make Quitman County free from venereal disease. County educational authorities aided by permitting teachers to devote classroom time to the program, while the pupils themselves distributed educational material to homes in the county.

Public meetings, organized by the investigator-educators and held in school buildings, churches, and lodge halls, constituted another method of venereal disease education. Usually two 15-minute films were shown, one entertaining and the other educational. Following the latter film, a lecture on syphilis was given by a doctor, nurse, or investigator-educator, utilizing a group of Kodachrome slides. These meetings were conducted throughout the county and took place at least twice each month.

The entire educational program emphasized the cause, spread, and cure of syphilis. Information on the symptoms of early syphilis, late manifestations of the disease, and the advisability of periodic blood tests was contained in the literature. Each person diagnosed as infected was given a personal explanation of his venereal disease—its cause, symptoms, and cure.

Contact Investigation

All persons who were tentatively diagnosed by the project clinician as having primary or secondary syphilis were interviewed immediately for contacts by the investigator-educator and again at the rapid treatment center at the time of the final diagnosis. Patients with early latent and other stages of syphilis were interviewed after the establishment of the diagnosis. Although investigation of primary and secondary syphilis contacts was given priority, the contacts of patients with early latent and other stages of syphilis were also followed. A detailed analysis of the contact investigation phase of the program will be presented in a subsequent report.

Routine Blood Testing

At the request of several of the larger plantation owners, workers were routinely blood-tested for syphilis during the project.

Results of Study

During the 10 months of the project almost 6,000 persons were examined for venereal disease in Quitman County. Approximately 4,000 volunteered for examination, 1,000 were blood-tested on plantations, and 564 were contacts of known cases (table 1). Venereal disease was identified in 1,483 persons, of which 455 were previously known to treatment. Thus, over 1,000 cases of previously unknown venereal disease were discovered and placed under treatment during the 10 months of this project. One hundred and eight cases of primary and secondary syphilis were discovered,

Table 1.—*Results of case finding in Quitman County, September 1947 through June 1948*

	Case-finding method			
	All methods	Voluntary reporting	Contact investigation	Blood testing
Persons examined [1]	5,795	4,101	564	1,130
Persons identified as infected	1,483	996	238	249
Gonorrhea	209	195	12	2
Syphilis	1,257	786	224	247
Other venereal diseases	17	15	2	0
Syphilis patients brought to treatment as a result of this examination	802	531	104	167
Primary and secondary	108	63	38	7
Early latent	167	102	32	33
Other syphilis	527	366	34	127

[1] Includes only persons on whom examinations were completed (120 investigations pending as of Sept. 1, 1948).

of which 63 came in of their own initiative (either because of symptoms, previous knowledge of the disease, or current information programs); 38, through contact investigation; and 7, through blood testing on plantations.

Table 2 compares the discovery rate of venereal disease in Quitman County with that in Humphreys County, which was chosen as a control because of its similarity to Quitman County in the method of case finding prior to the initiation of the project. During the project period, the normal routine of venereal disease case finding was continued in Humphreys County. It will be noted that while the discovery rate of venereal disease in Quitman County increased almost 300 percent during the period of the project, over a similar period in a previous year the discovery rate in the control county decreased approximately 40 percent. This increase in the discovery rate of syphilis in Quitman County during this period is all the more noteworthy because of the decline in early infectious syphilis noticed in most of the United States, including Mississippi and the control county, during the same period. The doubling of the discovery rate of primary and secondary syphilis in Quitman County is believed to be a striking improvement in case finding.

It is not known how many of the 43 cases of primary and secondary syphilis discovered in 1947 came in of their own accord, but even if they all did so, the number reporting voluntarily increased during the project period. Presumably, the information disseminated during the project paid off.

Discussion

It is the feeling of the Mississippi State Board of Health that this project demonstrated that venereal disease case finding can be carried out effectively in a

Table 2.—*Cases of venereal disease diagnosed in Quitman County and a control county during the period September 1947 through June 1948, compared with similar data for the previous year*

Cases brought to treatment	Quitman County			Control County		
	September 1946 through June 1947	September 1947 through June 1948	Percentage change	September 1946 through June 1947	September 1947 through June 1948	Percentage change
All venereal diseases	207	822	+297	320	191	−40
Gonorrhea	45	236	+424	129	71	−45
Syphilis	159	566	+256	180	111	−38
Primary and secondary	43	89	+107	75	37	−51
Early latent	69	115	+67	60	42	−30
Congenital	8	58	+625	6	10	+67
Other	39	304	+679	39	22	−44
Other venereal diseases	3	20	+567	11	9	−18

county with previously inadequate facilities.

Two other important developments were an outgrowth of this program:

1. The expansion of the Quitman County Health Department from an inadequately staffed, very limited health unit into a well-staffed, extremely active facility, employing a full-time health officer, a sanitation supervisor, a venereal disease investigator-educator, a clerk, and two nurses, and operating under a well-balanced general health program geared to provide adequately all types of health service.

2. As a result of increased community interest, the duties of the venereal disease investigator were expanded to include educational responsibility. During the project the functions of investigation and information complemented each other so effectively that all Mississippi investigators are now required to do venereal disease education on both an individual and a mass basis.

Summary

This report describes the planning, operation, and results of a venereal disease case-finding project, conducted in a rural area, which utilized the combined case-finding methods of contact investigation, venereal disease education, and a small amount of mass blood testing.

The following facts were disclosed:

1. A total of 1,483 persons was identified as infected with venereal disease in Quitman County during the 10 months of the project.

2. Eight hundred and two persons were brought to treatment with syphilis, 108 being in the primary or secondary stage of infection.

3. Of these 1,483 persons with venereal disease, 238 were contacts, 996 were clinic volunteers, and 249 were plantation workers.

4. Whereas venereal disease case finding in a control county decreased 40 percent during the project period, the number of cases of venereal disease diagnosed in Quitman County increased approximately 300 percent.

5. The accomplishment by investigators of venereal disease education in addition to intensive contact investigation led to the adoption of the present State policy of assigning venereal disease educational responsibility to all investigators.

Socioeconomic Factors in Syphilis Prevalence, Savannah, Georgia

C. D. Bowdoin, M. D., M. P. H.;[1] **Clair A. Henderson, M. D.;**[2] **Warren T. Davis, Jr., Health Program Representative;**[3] **John W. Morse, Biostatistician;**[3] **and Quentin R. Remein, Health Program Analyst**[3]

In the past few years there has been considerable discussion of the relationship between syphilis prevalence and socioeconomic factors. This study presents several aspects of this relationship as revealed by data collected during a mass blood-testing program conducted from October 15 to November 30, 1945, in Savannah, Ga.

While it is realized that blood test results are not necessarily identical with syphilis prevalence, there is a certain degree of association. Accordingly, the available data on the percentage of persons with a positive blood test, among the number of persons tested (exclusive of doubtful or unsatisfactory results), have been used in this analysis and will be referred to as the syphilis "prevalence" rate.

In this program, each person blood-tested was interviewed to obtain socioeconomic data beyond the usual identifying information; in addition, socioeconomic data taken from the 1940 census were employed. During the 45-day period of the program, 71,642 persons were tested; of these, 63,813 were included in this study, the remaining 7,829 being excluded because of doubtful or unsatisfactory results (table 1). The distribution of persons in this study was found to be fairly representative within race-sex groups of the population, judged by comparison with other available data (see appendix).

Table 1.—*Number of persons included in study and the percentage of such persons with a positive blood test, by race and sex*

Race and sex	Number of persons included in study	Percentage of persons with a positive blood test
White:		
Male	12, 402	3. 4
Female	13, 937	2. 3
Nonwhite:		
Male	16, 602	31. 5
Female	20, 872	30. 3

In relating socioeconomic factors to the syphilis "prevalence" rate, the following facts were disclosed: The rate was higher for married persons than for single persons in the younger age groups, whereas the reverse was true in the older groups; among those individuals 25 years of age and over, the fewer the school years completed, the more likely a person was to have syphilis (as measured by a positive blood test); certain differences were seen in "prevalence" rates by occupation; and low levels of socioeconomic conditions were associated with a high rate, much of the difference between the white and nonwhite syphilis "prevalence" rates being associated with differences in socioeconomic conditions.

Marital status, school years completed, and occupation will be discussed separately, followed by a joint consideration of the relationship between the syphilis "prevalence" rate and such socioeconomic factors as home ownership, monthly rental, racial composition of the population, water facilities, possession of a telephone, and school years completed.

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[1] Director, Division of Venereal Disease Control, Georgia Department of Public Health, Atlanta, Ga.; Special Consultant to U. S. Pub-ic Health Service.

[2] Commissioner of Health, Savannah-Chatham County Health Department, Savannah, Ga.

[3] U. S. Public Health Service.

Marital Status

Table 2 shows the ranking of marital status groups according to the syphilis "prevalence" rate for each race-sex group of persons 15 years of age and over. The divorced and separated group had the highest rate in all race-sex groups, with the exception of the white males, among whom the widowed group ranked highest. Persons who had been married but who were not living with spouse (separated, divorced, and widowed), had a higher rate than that of persons who were married or single. The married group presented the lowest rate in all race-sex groups, with the exception of the white females, among whom the rate was lowest for the single group.

Figure 1 shows the syphilis "prevalence" rates of marital status groups by race, sex, and age. For each race-sex group at the early ages, the rate for married persons was higher than that for single persons, but by the age of 25 (with the exception of white females) the situation was reversed, the rate for single persons becoming higher than that for married persons—a condition which did not change in the older age groups. Figure 1 also shows that the rates were higher for young persons (up to the age of 25) who were married, divorced, or separated than for single persons of the same age.

Table 2.—***Ranking of marital status groups according to syphilis "prevalence" rate***

White males		White females		Nonwhite males		Nonwhite females	
Marital status	Rate/100	Marital status	Rate/100	Marital status	Rate/100	Marital status	Rate/100
Widowed	9.6	Divorced or separated.	7.1	Divorced or separated.	44.7	Divorced or separated.	43.7
Divorced or separated.	7.0	Widowed	3.6	Widowed	41.5	Widowed	43.4
Single	4.4	Married	2.6	Single	38.9	Single	36.6
Married	3.2	Single	1.4	Married	35.6	Married	32.3

NOTE: Figures shown refer to the "prevalence" rates adjusted for the age distribution of all persons tested (15 years of age and over).

School Years Completed

In this paper, the analysis of schooling and the syphilis "prevalence" rate was limited to individuals 25 years of age and over, since these persons were considered to have established their patterns of schooling.

Two approaches were used. One method was to compare the median number of school years completed by persons with positive and with negative blood tests (table 3). It is seen that slightly more years of schooling were completed by the group with a negative blood test than by the group with a positive blood test.

The other method of analyzing schooling is shown in figure 2, which reveals that, in general, the rate became lower successively for those who completed more school years. This was true for all race-sex groups. A similar analysis for a specific age group disclosed the same general relationship. Apparently, the fewer the school years completed, the more likely a person, 25 years of age and over, was to have syphilis (as measured by a positive blood test).

Occupational Status

Results by occupational status are presented for employed persons and for persons not in employment status; occupational groupings for the former are

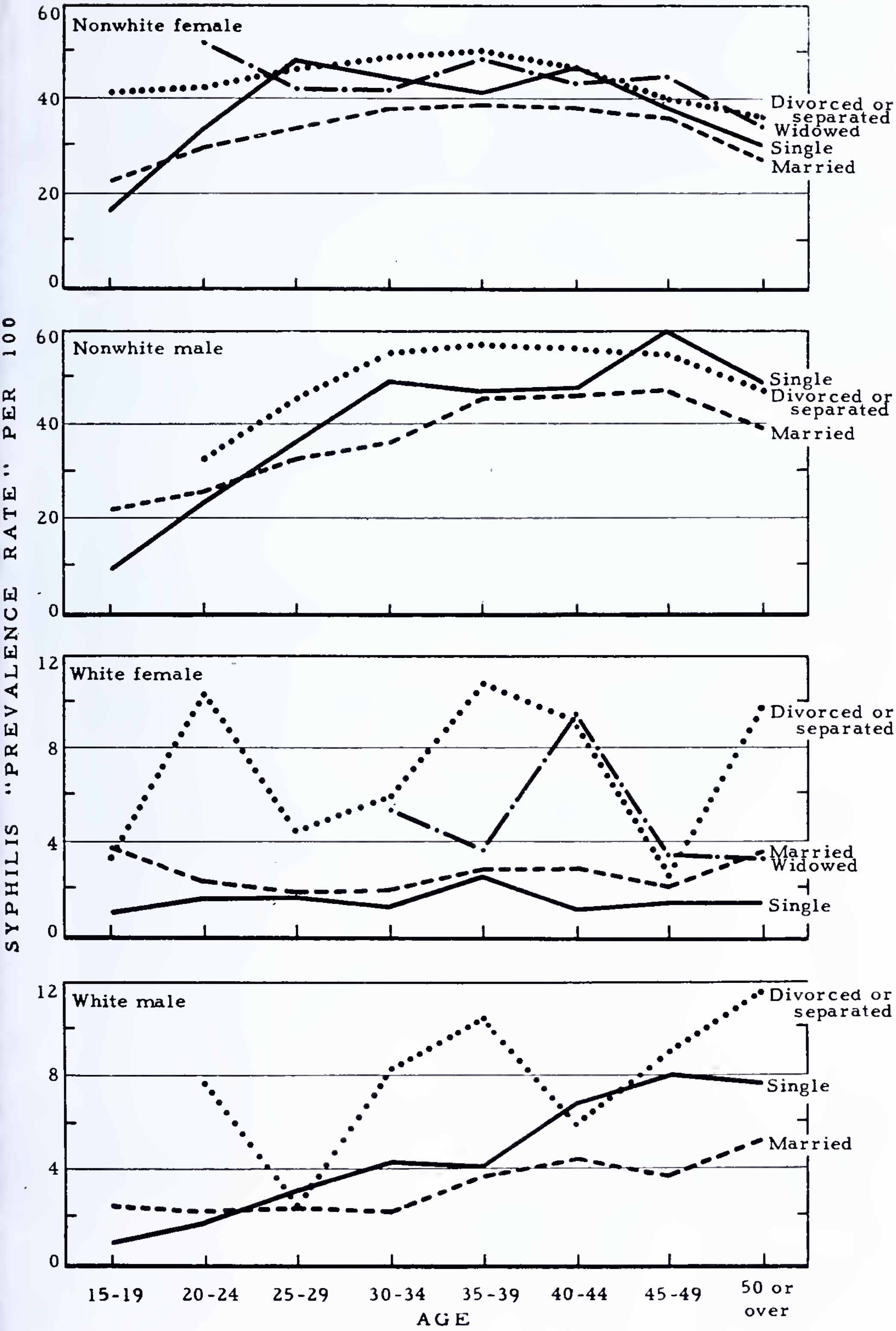

FIGURE 1.—Syphilis "prevalence" rates, by marital status, race, sex, and age.

Table 3.—*Comparison of the median number of school years completed by persons with positive and with negative blood tests, by race and sex*

Race and sex	Median number of school years completed by persons with a positive blood test	Median number of school years completed by persons with a negative blood test
White:		
Male	8.4	9.4
Female	8.7	11.0
Nonwhite:		
Male	4.2	4.5
Female	5.4	6.1

those used in census enumeration. Results are shown for the age groups 15 to 29, and 30 and over, since some occupations are characteristic of specific age groups.

Table 4 shows the syphilis "prevalence" rate for employed persons by occupation, age group, race, and sex. Also shown is the total number of persons in each group on which the rates were based.

In all race-sex-age groups, relatively low "prevalence" rates are seen among the professional, clerical, sales, and kindred workers (the so-called white-collar workers). Domestic service workers were the only occupational group who showed a consistently high rate. Both white and nonwhite male laborers 30 years of age and over showed a rate which was high for their respective race-sex-age groups. Greater differences might have been observed had the occupational classification been less broad and thus more indicative of socioeconomic conditions.

Table 5 shows the "prevalence" rate for each group of persons not in employment status. The rate of the prisoner group, which was the highest in all race-sex-age groups, was significantly higher than the

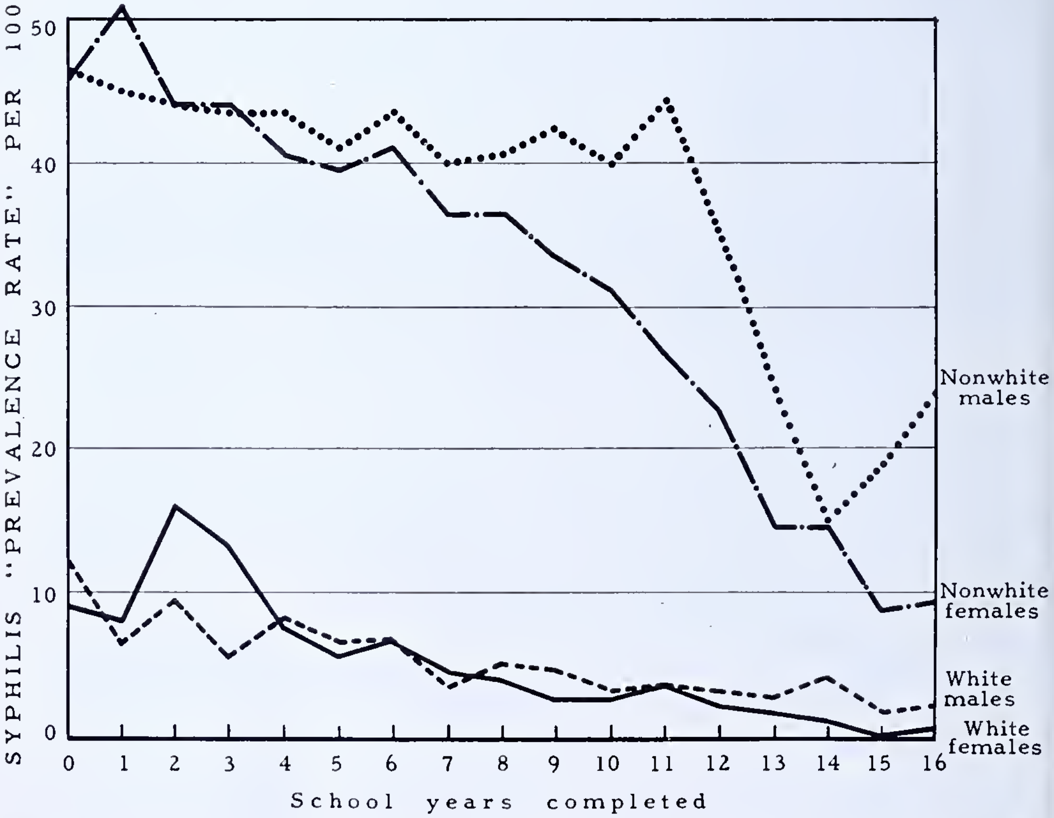

FIGURE 2.—Syphilis "prevalence" rates of persons 25 years of age and over, by number of school years completed, race, and sex.

Table 4.—*Syphilis "prevalence" rate for employed persons, by occupation, race, sex, and age*

Occupational status	Whites				Nonwhites			
	Males		Females		Males		Females	
	15–29	30 and over	15–29	30 and over	15–29	30 and over	15–29	30 and over
	Syphilis "prevalence" rate per 100							
Professional workers	0.0	2.5	1.2	0.5	20.3	36.4	26.0	25.0
Proprietors, managers, and officials	2.2	3.5	2.0	1.8	31.6	39.3	45.8	31.4
Clerical, sales, and kindred workers	.7	3.2	1.5	2.0	22.4	35.4	24.7	30.3
Craftsmen, foremen, and kindred workers	2.3	4.7	2.3	3.2	23.2	41.9	12.5	26.0
Operative and kindred workers	2.3	4.4	3.9	5.8	24.5	45.1	38.8	40.0
Domestic service workers	--------	--------	8.0	16.9	10.0	43.5	40.0	44.7
Service workers (except domestic)	1.0	5.2	4.1	3.7	24.7	41.5	30.5	36.7
Laborers	1.1	5.3	5.1	2.1	25.6	45.4	35.1	40.1
Total	1.8	4.2	2.2	2.9	24.9	43.9	36.2	41.5
	Total number of persons upon which the above rates are based							
Professional workers	136	443	242	372	59	228	192	192
Proprietors, managers, and officials	91	906	50	163	57	262	24	102
Clerical, sales, and kindred workers	279	1,248	1,717	1,130	98	243	97	132
Craftsmen, foremen, and kindred workers	699	3,087	86	125	327	1,004	32	50
Operative and kindred workers	736	1,568	466	329	877	1,729	374	678
Domestic service workers	0	4	25	65	20	62	1,706	3,415
Service workers (except domestic)	100	384	221	188	352	745	639	610
Laborers	93	247	39	47	1,754	4,356	370	394
Total	2,134	7,887	2,846	2,419	3,544	8,629	3,434	5,573

Table 5.—*Syphilis "prevalence" rate for persons not in employment status, by occupational status, race, sex, and age*

[By number of persons and rate per 100]

Occupational status	Whites				Nonwhites			
	Males		Females		Males		Females	
	15–29	30 and over	15–29	30 and over	15–29	30 and over	15–29	30 and over
	Syphilis "prevalence" rates per 100							
Students	0.7	--------	0.6	--------	5.9	--------	8.3	--------
Housewives	--------	--------	1.9	2.8	--------	--------	27.9	34.6
Unemployed persons	1.8	9.5	2.3	5.2	13.5	38.3	33.4	35.6
Prisoners	45.5	20.0	--------	--------	33.3	67.2	75.0	85.7
Private income and pensions	--------	7.3	11.1	6.5	16.7	47.6	71.4	32.0
Total	1.3	9.8	1.5	3.0	11.2	44.0	24.3	34.8
	Total number of persons upon which the above rates are based							
Students	936	0	1,128	0	559	0	1,081	0
Housewives	0	0	1,925	4,374	0	0	2,518	3,177
Unemployed persons	114	210	172	134	192	311	799	792
Prisoners	11	25	0	0	111	61	12	7
Private income and pensions	2	82	9	62	6	103	7	122
Total	1,063	317	3,234	4,570	868	475	4,417	4,098

average of all persons tested in Savannah.[4] Students, appearing in the 15 to 29 age group only, showed the lowest rate in that age group, significantly lower than the average for all groups.[4]

Six Socioeconomic Factors Considered Simultaneously

Socioeconomic conditions are here represented by the following factors: Home ownership, monthly rental, racial composition of the population, water facilities, possession of a telephone, and school years completed.[5] The relationship of syphilis prevalence to socioeconomic status was studied by the correlation technics described in the appendix. In each group, high "prevalence" rates were found to be associated with low levels of socioeconomic conditions, a relationship which was closer among nonwhites than among whites for both males and females. The relationship was closer among females than among males in each race group.

As shown earlier, there was considerable disparity in "prevalence" rates between nonwhite and white persons, the nonwhite male rate being approximately 9 times the white male rate and the nonwhite female rate being about 16 times the white female rate. However, when the socioeconomic conditions of nonwhite persons were made the same as those for whites by a mathematical technic described in the appendix, a considerable portion of the difference between the "prevalence" rates of the two races disappeared. Table 6 shows that the "prevalence" rates for nonwhite males and nonwhite females were decreased by 36 and 86 percent, respectively.

It will be noted that although the nonwhite rate was brought closer to the white rate by changing socioeconomic conditions, the nonwhite rate remained the higher. This difference may be due in part to not having used data that completely reflected socioeconomic status. Too, the larger reservoir of infection in the nonwhite group was itself a factor which could not be evaluated in the type of nongradual change made. The fact is that, although a difference in the "prevalence" rates remained, the disparity of the white and nonwhite rates was associated with differences in socioeconomic conditions.

Table 6.—*Effect on syphilis "prevalence" rates if nonwhite socioeconomic conditions are changed to those of whites*

	Rate per 100	Percent decrease in rate
Nonwhite males:		
Actual rate	43.5	36
Estimated rate after change to conditions of white males	27.9	
Nonwhite females:		
Actual rate	40.4	86
Estimated rate after change to conditions of white females	5.8	
White males: Actual rate	4.9	----------
White females: Actual rate	2.5	----------

Summary

The results of this study of the relationship between syphilis prevalence and socioeconomic factors in Savannah, Ga., may be summarized as follows:

1. The syphilis "prevalence" rate was higher for divorced, separated, and widowed persons than for married and single persons. Moreover, for all race-sex groups in the younger ages, the rate was higher for married persons than for single persons; by the age of 25, however, the rate became higher for single persons (with the exception of white females) than for married persons, and remained so in all older age groups (table 2 and fig. 1).

2. For those 25 years of age and over, the fewer the school years completed, the more likely a person was to have syphilis (as measured by a positive blood test) (table 3 and fig. 2).

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[4] Significant at the 1-percent level.

[5] Marital status and occupational status have been excluded from this part of the analysis because of the impracticability of using attributes of manifold classification.

3. Differences were noted in "prevalence" rates by occupational status. Prisoners in all race-sex groups (except the white female group in which there were no prisoners) had the highest rate. The domestic service group, which included a fairly large number of nonwhite females, had a relatively high rate. The rates were generally lower for students and for white-collar workers than for other groups (tables 4 and 5).

4. In general, a high "prevalence" rate was found to be closely associated with a low level of socioeconomic conditions.

Appendix

Representativeness of Data

A check on the representativeness of the study data was made to determine whether there was any bias which would invalidate the correlations and group comparisons. The data in the 1940 census, the only available source of information, were compared with study data as summarized below.

1. *Percentage of the population tested.*—The estimated percentage of the population tested (using the 1940 census as a base) was considerably lower for white than for nonwhite persons as shown by the following table for individuals 25 years of age and over.

Race and sex	Percentage of 1940 population tested
White:	
Male	37.5
Female	37.7
Nonwhite:	
Male	92.7
Female	90.1
Total	61.1

At least a quarter of the population (using the 1940 census as a base) was tested in each census tract (*1, 2*).

2. *Age.*—Differences in the age distribution between persons in the 1940 Savannah census and persons tested in 1945 closely paralleled changes in the age distribution of the civilian population of the United States between those years (*3*). There were proportionately fewer white and nonwhite males 15 to 34 years of age in 1945. This situation was almost exactly paralleled by Nation-wide changes and is probably due to the presence of males in the armed forces. Relatively fewer white females over 45 years of age were tested than would be expected on the basis of Nation-wide changes and changes in the 1940 population of Savannah (probably due to the fact that the program appealed less to older than to younger white women). The distribution by age of nonwhite females, however, was very close to both the national and Savannah population distribution.

3. *Marital status.*—In almost every age-race-sex group 15 years of age and over (by 5-year groups), proportionately more married and fewer single persons were tested than were enumerated in the 1940 census.

4. *School years completed.*—With respect to school years completed, the differences noted in the distribution of persons tested in each race-sex group compared with the distribution of persons in the 1940 Savannah population were similar to the changes in the national population from 1940 to 1947 (*4*). A study of the median number of school years completed by persons residing in each census tract for both the 1940 population and for persons tested in 1945 revealed that tracts with a high median in 1940 also had a high median for persons tested (and vice versa); however, the tract medians for persons tested were consistently higher than were the tract medians for the 1940 population. This was true for each race-sex group. This would lead to the conclusion that, although the levels have changed slightly, areas within the city maintained the same position relative to each other among persons tested as in the 1940 population.

5. *Occupation.*—Many differences were observed between the persons tested and the 1940 population in regard to occupational status. In the white male group, relatively more craftsmen and operatives,

but fewer clerks, salesmen, service workers, students, and unemployed persons were found among the persons tested than in the 1940 population; among white females, the tested group contained relatively more clerks, craftsmen, and operatives, but fewer housewives, students, and unemployed persons.

Among nonwhite males, there were relatively more craftsmen, operatives, and laborers, but fewer service workers, domestics, students, and unemployed persons; among nonwhite females, relatively more clerks, craftsmen, operatives, service workers, and laborers, but fewer students and housewives were observed. These were changes to be expected in a city devoted to shipbuilding and other war production and very likely were not due to disproportionate blood testing in the community (*1, 2*).

Correlation Methodology

The study of socioeconomic conditions in relation to syphilis prevalence was accomplished through the use of census tracts, which are defined as small areas, usually containing three to six thousand persons, into which certain large cities are subdivided. These tracts are fairly homogeneous in population characteristics and approximately uniform in size, taking natural barriers into consideration.

From information about residence obtained during the program interview, data on persons tested were classified according to the census tract of residence of these persons. Census tracts included in this study were those in which 30 or more persons in any particular race-sex group were tested, the average number of persons tested per tract being approximately 1,150. From 22 to 25 such tracts were used (depending upon the race-sex group). Only individuals 25 years of age and over were studied, since these were considered to have completed their schooling pattern and to have taken a responsible place in the socioeconomic pattern of their particular area or community.

The syphilis "prevalence" rate was computed for each tract by race-sex groups. The percentage of persons with home telephones was obtained from program interview data, while the other socioeconomic factors were summarized from census data by tracts as follows: The percentage of homes owner-occupied by each race group; the median monthly rentals of homes occupied by each race group; percentage of nonwhite persons in each sex group; the percentage of homes with running water occupied by each race group; and the median number of school years completed by persons in each race-sex group (*1, 2*). Age was not considered as a factor, because it was found that variations in age had little effect on the correlations for any race-sex group.

The results of this study, based on the testing of 33,653 persons 25 years of age and over with known Savannah addresses, disclosed "prevalence" rates in the various census tracts which ranged from 0 to 13.3 per 100 for white persons and from 26.2 to 65.3 per 100 for nonwhite persons.

Figure 3 summarizes the types of association (direct and inverse) observed between "prevalence" rates and socioeconomic factors and between the various socioeconomic factors. For each race-sex group, the relationship between "prevalence" rate and each of the factors used to measure socioeconomic conditions showed that a low socioeconomic level is associated with a high rate. The relationship between the various socioeconomic factors, however, was generally such that if one factor showed a high socioeconomic level, the other factors did also.

In order to determine how closely census tract "prevalence" rates were associated with socioeconomic conditions in general, the rates for each race-sex group were correlated with all the factors representing socioeconomic conditions. The coefficients of multiple correlation (R) were as follows:

White males:	$R=0.69$
White females:	$R=0.71$
Nonwhite males:	$R=0.77$
Nonwhite females:	$R=0.82$

It can be seen from these coefficients that

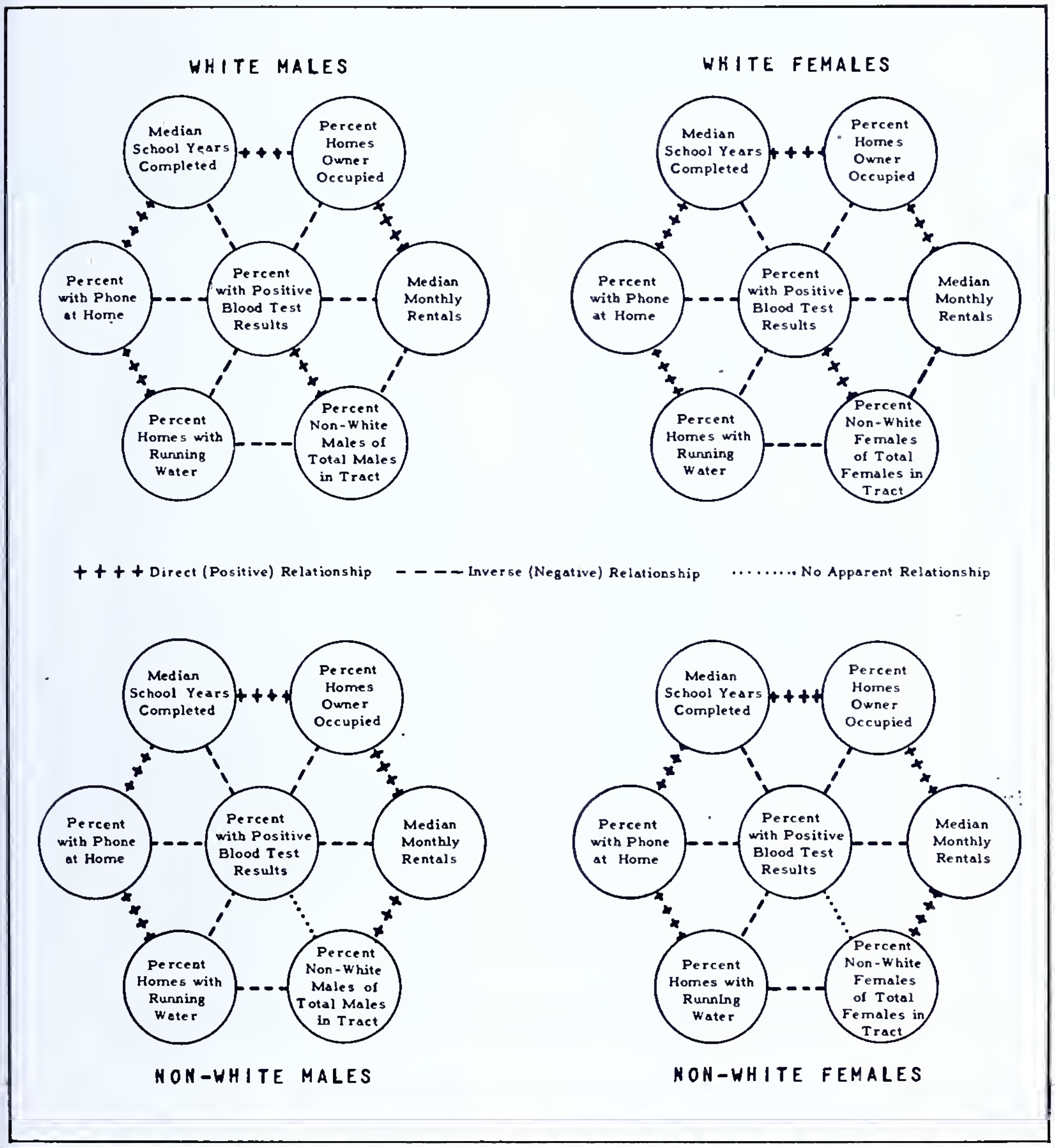
WHITE MALES
WHITE FEMALES
Median School Years Completed
Percent Homes Owner Occupied
Percent with Phone at Home
Percent with Positive Blood Test Results
Median Monthly Rentals
Percent Homes with Running Water
Percent Non-White Males of Total Males in Tract
Percent Non-White Females of Total Females in Tract
+ + + + Direct (Positive) Relationship
– – – – Inverse (Negative) Relationship
.... No Apparent Relationship
NON-WHITE MALES
NON-WHITE FEMALES

FIGURE 3.—Interrelationships: socioeconomic factors and syphilis "prevalence" rates.

in each case a close correlation existed between the "prevalence" rate and socioeconomic conditions and that this relationship was closer for nonwhites than for whites and closer for females than for males.

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Contact Investigation of Syphilis [1]

Joseph S. Spoto, Senior Surgeon, and Albert P. Iskrant, Principal Statistician, United States Public Health Service

Contact investigation of syphilis includes all the processes involved in obtaining from infectious syphilis cases the names of all persons from whom the patient may have acquired syphilis or to whom the patient may have given syphilis, examining such contacts, and placing them under treatment if indicated. Contact investigation is sometimes called "applied epidemiology" or the "direct epidemiologic approach."

Essentially, there are three basic methods of case finding: screen testing, public information, and contact investigation. It is not the purpose of this paper to discuss the relative effectiveness of contact investigation against public information, education, or other types of case finding. Factors such as aroused communities, public support, and so forth, cannot be measured in terms of cases of primary and secondary syphilis found. Moreover, contact investigation operates within chains of infection, and, unless links in these chains are made available for interview by other methods of case finding, contact investigation cannot work. We do intend, however, to present the case for the importance of investigation in the case-finding program. If everyone who developed syphilis reported promptly to a physician for diagnosis, obviously contact investigation or other administrative activity in case finding would not be necessary. Unfortunately, people do not do so. By the time most cases are diagnosed, there has been ample opportunity for wide dissemination of the disease.

Table 1 presents the data available to us as to why infected cases now come to treatment and why those who do not report voluntarily fail to do so.

Table 1.—*Distribution of cases of syphilis newly diagnosed in clinics, by stage of disease and reason for coming or for not coming to diagnosis*

	Percent		
Total cases diagnosed	100.0		
Newly diagnosed in primary and secondary stages	34.8		
Reason for coming to diagnosis			
Total diagnosed in primary and secondary stages	100.0		
Came of own accord		64.0	
Administrative action other than contact investigation		12.0	
Contact investigation		24.0	
Reason for not coming to diagnosis [1]			
Total nonvolunteers with primary and secondary syphilis	100.0		
Had not noticed symptoms		24.0	
Had noticed symptoms before being asked to have an examination		76.0	
Reason for not responding:			
Don't know why, just put it off			12.2
Didn't think had anything			10.9
Thought it would go away by itself, self-treatment			9.6
Time, money, transportation difficulties, couldn't get away			9.6
Went to private doctor and was treated for other than VD			8.4
Didn't want others to know			4.5
Thought it was "itch," "poison ivy," etc			3.7
Previous blood test O. K., due for periodic blood test			3.3
Afraid, didn't want to go to hospital			2.8
Other reasons			1.4
Not answered			9.6

[1] 497 nonvolunteers with primary and secondary syphilis.

It is estimated that only about 35 percent of the cases of newly acquired syphilis come to treatment in the primary and secondary stages. This is, of course, a loose estimate, since we do not know how many cases occur; however, whether the true figure is 25 or 45 makes little difference. The important point is that there are many cases of acquired syphilis that are not diagnosed or treated in the open-lesion infectious stages. Some of the reasons are as follows:

1. A certain proportion of persons who acquire syphilis (data not available as

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[1] From the Division of Venereal Disease.

to what the proportion is) have no visible lesions of primary and secondary syphilis and so are diagnosed (if and when they are diagnosed) as cases of early latent or late syphilis. This proportion is possibly low for males. These particular types of cases may come to treatment voluntarily because of periodic blood testing, but probably not until the infection is of rather long duration.

2. Of those who do develop syphilitic lesions, a certain proportion do not notice them. In our data, this proportion is 24 percent, but it should be emphasized that the figures apply only to nonvolunteers.

3. Some people develop symptoms of primary or secondary syphilis, notice them, but do not overcome a resistance to coming to diagnosis in order to "know for sure." The problem of overcoming resistance is not confined to the case finding of syphilis, but is probably common to most diseases. Although apathy is given as the chief reason in a group of 497 nonvolunteers (table 1), it is probable that fear of some description is more important than the data show. These data were summarized from reasons given by patients in their own words and not through the checking of boxes in predetermined questions. Studies of this type are valuable insofar as the information is used by those planning public information programs directed toward breaking down this resistance.

4. Already noted is the tendency of venereal disease patients to lapse from treatment even when presumably exposed to education in the clinic. This was a particular problem under the old routine arsenical treatment. Now observed, however, is a resistance in persons with syphilis reinfection or relapse to return for diagnosis or treatment. Although the evidence available is conflicting as to whether persons with repeat episodes of syphilis volunteer to a greater extent than persons with first episodes, it is clear that a large proportion of patients with repeat episodes do not come to diagnosis and treatment voluntarily.

The inescapable conclusion is that some type of administrative activity is usually necessary to bring cases of early, open-lesion syphilis to diagnosis and treatment whether or not the infection is a repeat episode. Contact investigation is the outstanding administrative tool for this purpose.

It may be well, then, to review the data available as to what contact investigation is actually accomplishing and what are its potentialities. Table 2 contains the indices calculated for the eight areas for which these data are available since early in 1944. Although these indices, like all other statistics calculated from operating data, are subject to errors of omission and commission, it is believed that, in general, the data do reflect the performance of these health departments included in the tabulation.

With but few exceptions, there has been a slow, gradual, consistent improvement in the accomplishments of contact investigation in these areas over the past 4 years. This improvement, while not startling, is nevertheless steady in most areas. Table 2 also shows the percentage of improvement in the eight areas over the past 4 years. This improvement has been shown both in the interviewing for contacts and in the investigation of these contacts. Perhaps the most encouraging note is that the greatest improvement has been shown in the indices that "pay off"—that is, in contacts brought to treatment with early syphilis.

Perhaps even more encouraging are the results which can be shown in "special demonstrations." In table 3, the indices of the two demonstrations in contact investigation which have been completed are compared with the indices of those of all areas. It can be seen readily that the number of contacts reported per patient was considerably higher in these areas than the number obtained through routine performance, a superiority which was maintained and became more marked in other indices. Proportionately, twice as many cases of open-lesion syphilis were discovered in these areas as were obtained through routine performance in health departments. That the improvement was not due to the interviewing

Table 2.—*Contact investigation indices, July 1944 to June 1948*

[Based on previously untreated primary and secondary syphilis admissions]

[8 areas submitting data for the 4-year period]

Areas	6-month calendar periods								Percentage improvement 1944–48
	1944	1945		1946		1947		1948	
	2	1	2	1	2	1	2	1	
	Contact index [Contacts obtained per admission]								
									Percent
A	1.16	1.92	1.67	2.02	2.04	1.70	1.67	2.13	84
B	1.32	1.36	2.05	1.47	-------	-------	-------	1.68	27
C	1.09	1.69	1.97	1.79	1.69	1.38	1.34	1.60	47
D	1.23	1.43	1.19	1.54	.87	1.23	1.16	1.10	−11
E	1.56	2.70	2.68	2.37	2.01	1.90	2.18	2.22	42
F	1.62	1.79	2.12	2.38	1.63	-------	2.05	1.80	11
G	2.07	2.82	1.94	2.46	2.02	2.42	-------	1.43	−31
H	1.70	2.58	4.97	3.04	1.69	3.34	3.57	4.04	138
Total	1.38	-------	-------	-------	-------	-------	-------	2.09	51
	Epidemiologic index [Contacts infected with syphilis per admission]								
									Percent
A	0.32	0.54	0.43	0.51	0.44	0.39	0.51	0.72	125
B	.38	.37	.55	.37	-------	-------	-------	.44	16
C	.30	.52	.54	.52	.56	.57	.51	.59	97
D	.26	.34	.23	.32	.29	.49	.31	.41	58
E	.52	.80	.77	.74	.67	.67	.62	.70	35
F	.50	.51	.67	.82	.57	-------	.70	.72	44
G	.39	.39	.34	.45	.24	.20	-------	.24	−38
H	.55	.84	1.19	.66	.40	.68	.66	.90	64
Total	.37	-------	-------	-------	-------	-------	-------	.60	62
	Brought-to-treatment index [Contacts brought to treatment with syphilis per admission]								
									Percent
A	0.11	0.26	0.22	0.30	0.21	0.19	0.27	0.34	209
B	.14	.12	.30	.24	-------	-------	-------	.25	79
C	.22	.38	.39	.29	.24	.22	.22	.23	5
D	.10	.17	.10	.17	.14	.20	.16	.18	80
E	.23	.28	.29	.31	.28	.37	.32	.35	52
F	.22	.27	.33	.40	.30	-------	.39	.38	73
G	.21	.22	.17	.29	.11	.10	-------	.14	−33
H	.18	.36	.45	.28	.29	.40	.34	.53	194
Total	.16	-------	-------	-------	-------	-------	-------	.31	94
	Lesion-to-lesion index [Contacts brought to treatment with syphilis lesions per admission]								
									Percent
A	0.04	0.12	0.09	0.15	0.11	0.09	0.12	0.16	300
B	.07	.05	.17	.15	-------	-------	-------	.16	129
C	.15	.24	.27	.17	.14	.15	.13	.13	−13
D	.04	.08	.05	.07	.06	.10	.07	.09	125
E	.12	.12	.16	.19	.18	.16	.19	.20	67
F	.14	.12	.17	.18	.17	-------	.23	.26	86
G	.09	.08	.05	.10	.03	.04	-------	.05	−44
H	.07	.11	.17	.10	.13	.15	.11	.19	171
Total	0.8	-------	-------	-------	-------	-------	-------	.17	89

alone is shown by the following data: The percentage infected of contacts reported was almost 50 percent higher in the special demonstrations; the percentage of contacts reported who were brought to treatment in the primary and secondary stages was almost twice as high in the special demonstration areas. This indicates not only that more contacts are reported but also that a higher percentage of them are located and examined. These demonstrations are encouraging as it is believed that most areas could raise their performance to these figures if patients with early infectious syphilis were interviewed carefully for contacts and diligent follow-up instituted.

From time to time it has been mentioned that differences in contact indices from area to area may be due to the types of patients available for interview. While it is true that there are differences in results of interviewing between types of patients, these differences are minor compared to differences between areas, and they support former statements that the differences between areas are due to interviewing policies and performances within the area and not to the type of patient available for interview.

Table 3.—***Comparison of results of contact investigation in two special studies with the average accomplishments in health departments***

	Study A	Study B	Average, 27 areas having data January–June 1948
Number of primary and secondary syphilis cases diagnosed	89	201	16,480
Contact index	3.60	3.26	2.45
Epidemiologic index	1.62	1.61	.76
Brought-to-treatment index	.81	.83	.40
Lesion-to-lesion index	.40	.47	.19
Percentage of infections identified of contacts reported	45.0	49.4	31.1
Percentage of contacts reported brought to treatment in primary and secondary stage	11.4	14.4	7.7
Number of contacts necessary to find 1 primary or secondary syphilis case	9.0	6.9	12.9

Table 4.—***Contact indices: Average number of contacts named by patients with diagnosed cases of previously untreated primary and secondary syphilis***

[Special study results compared by patient characteristics]

Characteristics of patients	Contact indices				
	Total	White		Negro	
		Male	Female	Male	Female
Total	3.17	2.59	3.08	3.60	3.39
Age in years:					
15–29	3.33	2.72	3.38	3.72	3.35
30–44	2.59	2.46	2.14	2.93	3.30
Marital status:					
Single	3.58	2.65	3.83	3.84	4.03
Married	2.98	2.53	2.77	3.63	3.01
School years completed:					
Under 9	3.46	2.67	3.30	3.90	3.77
9 and over	3.08	2.53	2.96	3.47	3.39
Residence:					
Rural	3.44	2.74	2.81	4.01	3.85
Urban	3.13	2.53	3.34	3.47	3.15
Mobility:					
Transient	3.39	2.68	3.34	3.47	4.20
Stable	3.26	2.58	3.17	3.64	3.74

Table 4 shows contact indices for the various color, sex, and social groupings. It will be noted that, in general, white females give more contacts than white males, and Negroes, more than whites. It is important to note that these indices are averages and do not indicate what can be expected from any individual. For example, more white males named two contacts than did white females, and more white females named one contact than did white males. As may be expected, the higher average for white females was due to the number in this group who named 8, 9, 10, or more contacts. The pattern is different in the Negro group where, in general, the males indicate a high number of sexual partners. Young persons usually give more contacts than older persons; single, more than married; and persons with less schooling, more contacts than persons with more schooling. Except for white females, rural persons name more contacts than urban persons, and transient persons give more contacts than individuals of stable residence. To generalize, it can be said that young single persons with less than 9 years of schooling give more contacts than other persons.

In an effort to determine the factors which keep contact investigation from attaining its potentialities, the data and the description of projects by responsible investigators have been reviewed. The following would seem to be some of these factors:

1. Whose job is it to interview? One of the chief reasons for low contact indices is the large number of patients who go uninterviewed because of carelessness, confusion on the part of the staff as to whose function it is to interview, or the fact that the patient leaves the clinic without being made available for interview.

2. Much interviewing is done at rapid treatment centers. This, while desirable, does delay the process, introducing a spatial and temporal gap between the interviewer and the investigator. In general, contact investigation is done more effectively when interviewing, location, and examination are under the jurisdiction of the same person.

3. The multiple form for reporting contacts, is a means, not an end, and should not be a cause of delay in the transmission of information to investigators. While in many instances the form in itself may not be responsible for delay, its routing through the central registry and central investigating office causes delay in assignments. Persons responsible for contact investigation should consider the distribution of forms from the central registry as important as other phases of the contact investigation process.

4. There is increasing evidence that many of the differences in lesion-to-lesion indices are due to the quality of the examination for syphilis. In general, areas with high lesion indices find more primary and secondary syphilis among the contacts examined than do areas with low indices. Searching for lesions and repeat examinations of those not infected at the first examination are probably the two factors most important in this regard.

5. Division of authority of functions: It would seem that the check-back from the examining source to the interviewing source is important in successful contact investigation. With a division of authority between interviewing and investigation, the check-back becomes a rarity. For example, the patient reports a contact who is not infected at the time of the first examination. Obviously, the source contact was not obtained and the patient should be reinterviewed. If the investigator has only a form, he cannot know that this is the only contact and possibly he holds the form for 30, 60, or 90 days to determine the presence or absence of syphilis. When this form is eventually returned to the interviewing source, it is obviously too late to reinterview the patient; moreover, even if the patient were available for interview, much syphilis presumably will have been spread.

Summary

There has been a gradual, consistent improvement in the accomplishments of contact investigation in eight areas which have been studied since 1944: The contact index has gone up 51 percent; epidemiologic index, 62 percent; brought-to-treatment index, 94 percent; and lesion-to-lesion index, 89 percent. Two special demonstration areas discovered proportionately twice as many cases of open-lesion syphilis and 50 percent more infected contacts than were obtained through routine performance in health departments.

Contact indices show that, in general, young single persons with less than 9 years of schooling give the largest number of contacts.

Factors interfering with the full accomplishment of contact investigation include: separation in space and time of the functions of interviewing, location, and examination of contacts; delay in distribution of multiple forms from the central registry to investigators; quality of the examination for syphilis; and division of authority of the functions, leading to failure to reinterview patients whose contacts reveal no syphilis upon initial examination.

Sugar Fermentations of Gram-Negative Diplococci Isolated From the Genitourinary Tract of Penicillin-Treated Gonorrhea Patients[1]

Louis Wax, Bacteriologist [2]

The scarcity of reports in the literature on the occurrence of *Neisseria* other than the gonococcus in cultures of genitourinary exudates has led to the impression that such nonspecific *Neisseria* occur only infrequently in such exudates. In 1942, however, Carpenter and Charles (*1*) reported the isolation of *Neisseria meningitidis* from the genitourinary tract of 7 patients. These 7 cultures occurred among 103 strains of gram-negative diplococci isolated from gonorrhea cases or carriers. In 1943, Carpenter (*2*) reported the isolation of 3 strains of *Neisseria flava* from the genitourinary tract of 3 patients with clinical symptoms suggestive of gonococcal infection.

The purpose of this paper is to show that *Neisseria* with fermentation reactions other than those of the gonococcus are by no means infrequently encountered in cultures of genitourinary exudates and fluids.

Methods and Materials

The methods and materials used were essentially the same as those recommended by Carpenter (*3*). Prepared Difco mediums were used for cultivation and fermentation; however, sterile ascitic fluid was used for enrichment in all mediums, and tyrothricin to a final concentration of between 1:25,000 and 1:50,000 was used in the isolation plates.

Results

During the period July 1, 1946, to June 30, 1948, inclusive, 790 cultures from both male and female gonorrhea patients treated with penicillin in oil and beeswax were found to be positive for *Neisseria*. About 60 percent of these organisms were isolated in pure culture and their fermentation of at least dextrose, maltose, sucrose, and lactose determined. Approximately 81 percent of the isolated cultures fermented dextrose only and were reported as the gonococcus, while approximately 19 percent (11 percent of the total positives) were found to have biochemical reactions other than those of the gonococcus. Seven out of every ten of these nonspecific *Neisseria* fermented dextrose, maltose, and sucrose, but not lactose. Many could be classed as *Neisseria sicca* on the basis of the fermentation reactions when levulose and mannitol were added, except for the fact that a definite yellow pigment was frequently produced on Löffler's coagulated serum slants. The results obtained with this penicillin-treated group are presented in table 1.

In order to determine whether nonspecific *Neisseria* occur in genitourinary

Table 1.—*Fermentation reactions of* Neisseria *isolated from the genitourinary tract of gonorrhea patients previously treated with penicillin*

Group	Fermentation reactions [1]				Number of cultures
	Dextrose	Maltose	Sucrose	Lactose	
I	A	O	O	O	359
II	A	A	A	O	58
III	A	A	O	O	21
IV	O	O	O	O	4

[1] A represents visible acid produced.
O represents growth without visible acid production.

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[1] From the Division of Venereal Diseases, Department of Public Health, City and County of San Francisco.

[2] Department of Public Health, City and County of San Francisco.

NOTE.—The author is indebted to Richard A. Koch, M. D., Chief of the Division of Venereal Diseases, Department of Public Health, City and County of San Francisco, without whose interest and help the preparation of this paper would not have been possible.

exudates and fluids sent to the laboratory for diagnostic purposes rather than for purposes of follow-up of patients after penicillin therapy, 87 (26 from males and 61 from females) of 115 positive cultures were isolated and studied further by sugar fermentation. Since many urethral exudates positive by smear for intracellular gram-negative diplococci were not included in the study, no conclusions should be drawn from the results presented in table 2 as to the incidence of nonspecific *Neisseria* in diagnostic exudates. In the experience of the author, not a single profuse purulent urethral discharge in the male revealing intracellular gram-negative diplococci with flattened adjacent sides proved upon cultivation to be *Neisseria* other than the gonococcus; however, only a small number of cultures of this type were done. On the other hand, nonspecific *Neisseria* have been isolated from the male from atypical urethral discharges and from prostatic secretions in the absence of urethral discharges.

Table 2.—***Fermentation reactions of* Neisseria *isolated from the genitourinary tract of patients for purposes of diagnosis***

Group	Fermentation reactions [1]				Number of cultures
	Dextrose	Maltose	Sucrose	Lactose	
I	A	O	O	O	79
II	A	A	A	O	5
III	A	A	O	O	2
IV	O	O	O	O	1

[1] A represents visible acid production.
O represents growth without visible acid production.

Discussion

That the frequency of nonspecific *Neisseria* in cultures of genitourinary exudates and fluids constitutes a diagnostic and epidemiologic problem in the cultural follow-up of treated gonorrhea patients cannot be denied. It is assumed that the source of these organisms is the genitourinary tract; however, the possibility of accidental external contamination at the time that the specimens are obtained cannot be ignored. As yet there is no proof that *Neisseria* other than the gonococcus are pathogenic for the genitourinary tract. Since, according to Hehre and Hamilton (*4*), streptococci inhibit the development of *Neisseria* colonies, the frequent isolation of *Neisseria* other than the gonococcus may be explained in part by the in vivo inhibition of streptococci during penicillin therapy and in part by the use of tyrothricin in the culture mediums.

Summary

Seven hundred and ninety routine cultures from the genitourinary tracts of previously diagnosed male and female gonorrhea patients treated with penicillin revealed oxidase-positive colonies consisting of gram-negative diplococci. Of these, 442 were isolated in pure culture and their fermentation of dextrose, maltose, sucrose, and lactose determined. Three hundred and fifty-nine fermented dextrose only, while 83 produced other reactions in these sugars. None fermented lactose. Many of the nongonococcal strains produced a definite yellow pigment on Löffler's coagulated serum.

Nongonococcal strains of *Neisseria* occurred in cultures submitted for diagnostic purposes, but their incidence in such cultures was not ascertained.

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CURRENT LITERATURE

Note: Abstracts of any article listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is listed below.

Acta dermat.-venereol., Stockholm

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Am. Heart J., St. Louis

The terminal electrocardiogram: twenty-three case reports and a review of the literature. [Syphilis.] M. W. Stroud and H. S. Feil. 35: 910–923, June 1948.

Am. J. Hyg., Lancaster

*Factors affecting the survival of *Treponema pallidum* in vitro. Robert A. Nelson, Jr. 48: 120–132, July 1948.

Protective antibodies in the serum of syphilitic patients. Thomas B. Turner, Fred C. Kluth, Charlotte McLeod and Charles P. Winsor. 48: 173–181, Sept. 1948.

Factors affecting the survival of *Treponema pallidum* in vitro. Robert A. Nelson, Jr. Am. J. Hyg., 48: 120–132, 1948.

Quantitative experiments are described on physical and chemical factors affecting the survival of virulent *Treponema pallidum* in vitro. The study was undertaken as a rational approach toward cultivation, in the hope that the attainment of conditions optimal for survival would lead to growth and multiplication. Utilizing the medium and technics described in the article, it was possible to obtain survival of 50 percent of the organisms for 6 to 8 days. Survival appeared to be improved when rabbit testes were removed within the first 24 to 48 hours of clinically recognizable syphilitic orchitis. In order to avoid exposing the organisms to unfavorable pH levels, the medium was equilibrated with 5 percent CO_2 for at least 2 hours at the temperature to be used for incubation before the syphilitic testis was placed in it for extraction. The fluid medium of low viscosity used in the study is considered of particular value by the author in that characteristic motility can easily be ascertained.

Beneficial effects were noted when crystalline bovine albumin, 5 percent CO_2, inorganic phosphate, sodium pyruvate, glutathione, cysteine, and vitamins were included in the medium. In addition to this basal medium of known composition, a small concentration of tissue extract or serum ultrafiltrate appeared to be essential for survival.

Motile organisms retained their virulence, and half-life of the organisms was consistently prolonged for 6 to 8 days. Indications of growth, but not of multiplication, were obtained. An immobilizing action of crystalline penicillin G in low concentrations was reported, and suitable technics for testing new antibiotics and chemotherapeutic agents are described.

Am. J. Med., New York

*Current concepts of immunity in syphilis. Harold J. Magnuson. Symposium on Syphilis. 5: 641–654, Nov. 1948.

Current concepts of immunity in syphilis. Harold J. Magnuson. Symposium on Syphilis. Am. J. Med., 5: 641–654, 1948.

This article summarizes current knowledge of immunity in syphilis and reviews the pertinent experimental and clinical literature.

The advent of rapid treatment methods for syphilis has renewed interest in the problems of immunity. Natural immunity or resistance includes those factors not due to previous experience with the infecting organism which modify the susceptibility of the host to infection. There is no indication of a true racial immunity to syphilis in man, although evidence suggests that the course of the disease and the nature of clinical manifestations may show some variation. In the absence of inoculation experiments, it is impossible to assess accurately the degree to which natural immunity may occur in man. Recent studies have indicated that approximately 50 percent of the named contacts of primary and secondary syphilis apparently escaped infection.

Acquired immunity comprises that resistance to infection which is dependent upon the previous experience of the host with the same or related infecting organism. Factors involving the infecting organisms which appear to influence the course of acquired immunity include: strain of the organism, virulence of the organism (for the particular host), and size of the inoculum. Host factors include: duration of the original immunizing infection, site and manner of the first and second inoculations, and possibly the degree of systemic or local reaction to the original infection. The quantitative data suggest that asymptomatic reinfection represents a partial immunity sufficient to destroy the majority of the spirochetes so that no local lesion develops but insufficient to destroy all of the spirochetes.

There is some clinical evidence that infection with either yaws or syphilis may protect against the other of the two diseases, but cross inoculation experiments between yaws and syphilis in experimental animals have not shown the same results.

In most instances, search for the usual type of circulating antibodies in the mechanism of acquired immunity has proved unsuccessful. Reagin, the substance giving rise to positive complement-fixation and flocculation tests for syphilis, is a circulating antibody, but its relation to the immune process is most uncertain.

Many technics in attempted artificial immunization have resulted in the development of positive serologic tests for syphilis in the serum of experimental animals, but there has been no evidence of acquired immunity. The extent to which findings in experimental animals can be applied directly to humans is unknown. One fact which seems well established is that shortly after the onset of the primary lesion in humans a local immunity develops which prevents the development of a new lesion following reinoculation with *Treponema pallidum.*

The extent to which changes in immunity or in sexual environment may influence the current apparent failure or relapse rates in clinical syphilis cannot be ascertained. If acquired immunity in man develops in a progressive manner similar to that in the rabbit, one would expect that a previous infection with syphilis would modify a subsequent exposure to the disease.

Am. J. Nursing, New York

The modern treatment of venereal disease. Penicillin isn't always the answer. Theodore Rosenthal. 49: 93–94, Feb. 1949.

AM. J. OBST. & GYNEC., ST. LOUIS

Observations on vaginal absorption of penicillin. Stuart Abel, Chester J. Farmer and Jeanne Doucette. 55 : 461–468, Mar. 1948.

AM. J. PSYCHIAT., BALTIMORE

Neurosyphilis. Augustus S. Rose and Harry C. Solomon. 104 : 470–473, Jan. 1948.

New facts on prognosis in mental disease. [Syphilis.] Robert H. Israel and Nelson A. Johnson. 104 : 540–545, Mar. 1948.

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AM. J. SURG., NEW YORK

Cancer, gumma and tuberculosis of the forearm. Nelson C. Jefferson. 57 : 260–265, Feb. 1949.

AM. J. SYPH., GONOR. & VEN. DIS., ST. LOUIS

*The treatment of late symptomatic neurosyphilis at the Boston Psychopathic Hospital. A study of the results of penicillin therapy in 394 patients treated between February, 1944 and March, 1948. Israel Kopp, Augustus S. Rose and Harry C. Solomon. 32 : 509–520, Nov. 1948.

*Long-term results in neurosyphilis treated with penicillin alone. John H. Stokes, Mortimer S. Falk and George D. Gammon. 32 : 521–545, Nov. 1948.

*Neurosyphilis. Evaluation after two years of treatment with penicillin alone and with a combination of penicillin and malaria. Arthur C. Curtis, S. F. Horne and Dorothy H. Norton. 32 : 546–564, Nov. 1948.

*Spinal fluid and blood complement fixation reversal in neurosyphilis. Y. T. Wong and Henry Packer. 32 : 565–573, Nov. 1948.

*Syphilitic primary optic atrophy as a cause of blindness; importance of early diagnosis. Joseph V. Klauder, George P. Meyer and Benjamin A. Gross. 32 : 574–586, Nov. 1948.

*Acute syphilitic meningitis. A report of 80 cases. Osvaldo A. Pardo and Thomas W. Farmer. 32 : 587–598, Nov. 1948.

*Vagotomy in the treatment of gastric crises of tabes dorsalis. Charles W. Stoops, Jr., Leonard S. Markson, James M. Sullivan and Joseph Kanter. 32 : 599–603, Nov. 1948.

The treatment of late symptomatic neurosyphilis at the Boston Psychopathic Hospital. A study of the results of penicillin therapy in 394 patients treated between February, 1944 and March, 1948. Israel Kopp, Augustus S. Rose and Harry C. Solomon. Am. J. Syph., Gonor. & Ven. Dis., 32: 509–520, 1948.

The authors report on the penicillin treatment of 394 patients with neurosyphilis at the Boston Psychopathic Hospital from February 1, 1944, to March 1, 1948. Of 305 patients with general paresis, juvenile paresis, and taboparesis, 245 presented various psychoses, including the schizophrenic type of syndrome seen in 55 individuals.

Penicillin alone was administered to 94 patients and penicillin combined with fever was used in 300 cases. Fever therapy consisted of 5 to 7 paroxysms of malaria with temperature above 104° F. (rectal) or 20 hours of artificial fever above 105° F. Penicillin was administered before, during, or after fever and was increased in July 1945 from 3 million to 6 million units, given over intervals of 5 to 15 days. The clinical status of the 305 paretic patients followed for 3 months or more reveals that 170 (56 percent) have improved; 104 (34 percent) are unimproved; and 31 (10 percent) have died, death being attributable to syphilis in only 16, however.

The importance of the original clinical picture in the therapeutic results is shown in the improvement of 50 (85 percent) of 59 paretic patients without psychosis, given combined penicillin and fever therapy, as against improvement in only 117 (55 percent) of 211 psychotic patients, under the same therapy. As to type of psychosis, only 25 percent of 48 patients with a schizophrenic type improved, as against 60 percent, 65 percent, and 90 percent in the simple dementing, grandiose, and manic-depressive types, respectively.

Three million units of penicillin, administered over a 15-day period and combined with fever, gave better clinical results than when given for 10 days or less, clinical improvement resulting in 71 percent of 126 patients on the first schedule and in 58 percent of 79 patients on the latter, no significant difference being observed in the use of 3 million units as against 6 million units. Re-treatment was more frequent when 3 million units of penicillin were employed with or without fever and when penicillin was used alone, being necessary in 52 percent of 54 patients, in contrast to 21 percent of 219 patients receiving combined penicillin and fever therapy.

From this study the authors conclude that a short course of malaria therapy when added to penicillin given over a 15-day period is equal or superior to any treatment thus far known in late symptomatic neurosyphilis. Consideration of the type of psychosis in evaluating final therapeutic results is emphasized, however.

Long-term results in neurosyphilis treated with penicillin alone. John H. Stokes, Mortimer S. Falk and George D. Gammon. Am. J. Syph., Gonor. & Ven. Dis., 32: 521–545, 1948.

The authors report on the results of 537 patients studied by the Penicillin-Syphilis Panel at the University of Pennsylvania since 1943. All of these patients were treated for neurosyphilis with penicillin alone, and data presented in this report are on patients observed for 2 years or more. From observation of some of the patients for four or more years, the serial examinations of spinal fluids and parallel clinical data gave an impressive account of what penicillin actually has accomplished. The spinal fluid record of the original 39 patients, the first treated with penicillin in 1943, showed the spinal fluid to be normal, near-normal, or marked improvement. Thirty-two of these patients were followed from 3 to 4 years.

Forty-six percent of the patients with paresis, 60 percent of those with taboparesis, and 80 percent of those with tabes dorsalis with type III spinal fluids have achieved normal or near-normal spinal fluids. Sixty percent of the meningovascular and 74 percent of the asymptomatic neurosyphilis patients have achieved a similar status. These figures suggest the superiority in some types of neurosyphilis and equality in others of penicillin alone over malaria.

A series of case protocols is presented showing various types of response, success, and failure in the therapy of neurosyphilis with penicillin alone. Two life histories of neurosyphilis are presented which cover 22 and 26 years of observation of four types of therapy including routine, arsenic-heavy metal, malaria, tryparsamide, and penicillin.

The authors believe that penicillin is superior to other forms of treatment for all types of neurosyphilis, and it deserves first choice on the scores of safety, convenience, and effectiveness.

Neurosyphilis: Evaluation after two years of treatment with penicillin alone and with a combination of penicillin and malaria. Arthur C. Curtis, S. F. Horne and Dorothy H. Norton. Am. J. Syph., Gonor. & Ven. Dis., 32: 546–564, 1948.

A brief review of the literature concerning the treatment of neurosyphilis with penicillin alone and with a combination of penicillin and malaria is given. This report concerns 223 patients treated for some type of neurosyphilis who were observed for a minimum of 1 year subsequent to treatment. Of this number, 104 were followed for at least 2 years. There were 76 females and 147 males.

All of the patients received either penicillin alone or penicillin plus malaria. Penicillin was administered in saline, 40,000 units intramuscularly every 3 hours for 100 doses, making a total dosage of 4,000,000 units. For those receiving penicillin plus malaria, 50 or more hours of fever over 103.5° F. (rectal) was induced.

One year after treatment, the group of patients who received penicillin alone showed 79 percent clinical improvement and 82 percent improvement in the spinal fluid abnormalities. The group who received penicillin plus malaria attained 69 percent clinical improvement and 89 percent improvement in the spinal fluid findings. Twenty-two (21.5 percent) of the patients in the penicillin alone group and 14 (12.3 percent) in the combined therapy group had negative spinal fluid examinations at the end of the year. After a 2-year observation of 104 patients, 86 percent of the penicillin alone group showed clinical improvement, and 85 percent had spinal fluid improvement. The combined therapy group showed improvement of 66 percent clinically and 98 percent in spinal fluid findings. During the second year, seven patients of the penicillin alone group developed negative spinal fluid examinations, and in the combined therapy group three reverted to negativity.

The cerebrospinal fluid abnormalities comprise the most substantial basis for analysis of neurosyphilis patients. The group of patients with asymptomatic neurosyphilis permitted the most opportunity for a comparison of the effect of the two forms of therapy on the spinal fluid abnormalities. From the results, it was evident that the addition of therapeutic malaria did not enhance the efficacy of penicillin. Penicillin alone is the treatment of choice in asymptomatic neurosyphilis, as well as meningovascular syphilis and tabes dorsalis. As for general paresis, penicillin alone is less dangerous and probably equal in therapeutic effectiveness to the combined therapy.

Spinal fluid and blood complement fixation reversal in neurosyphilis. Y. T. Wong and Henry Packer. Am. J. Syph., Gonor. & Ven. Dis., 32: 565–573, 1948.

This article presents an analysis of reversals observed in the complement-fixation test in spinal fluid and blood in 120 patients with neurosyphilis following treatment with penicillin alone or penicillin and malaria. Of this group, 56 received penicillin alone, while 64 received a combination of penicillin and malaria. Penicillin was administered in the form of the sodium salt in saline solution in doses of 30,000 units every 3 hours. The average number of hours of fever above 103° F. (rectal) received by the penicillin-malaria group was 39.5. The Kolmer quantitative test was employed for spinal fluid complement-fixation studies, using spinal fluid in amounts ranging from 0.03125 cc. to 1.0 cc. The same test was employed for blood serologic studies, using dilutions from 1 : 2.5 to 1 : 80. Qualitative Kahn tests were performed simultaneously on the blood. Spinal fluid reversal was considered as achieved when reported as one plus or less in 1 cc. of spinal fluid. Blood serologic reversal was considered as a negative or doubtful reaction in the lowest dilution of the quantitative test and in the qualitative Kahn test.

The proportion of patients with paresis or taboparesis in the penicillin-malaria group was 64 percent, while the proportion in the penicillin group was 52 percent. The proportion with meningovascular neurosyphilis was 30 percent in the total penicillin group and 19 percent in the total penicillin-malaria group. The average follow-up period for both groups was 18.9 months.

The spinal fluid reversal occurred in 30 percent of the total group over the period of observation. The proportion of reversals was 51.7 percent for the meningovascular group, 22.9 percent for the paresis and taboparesis group, and 23.8 percent in the tabes dorsalis group. For the two treatment categories, a higher proportion of the group receiving penicillin alone (33.9 percent) showed reversal than for the penicillin-malaria group (26.6 percent).

The proportion of the total group achieving blood serologic reversal was 20 percent. The highest proportion was contributed by the meningovascular group with a rate of 34.6 percent. A higher proportion of reversals was observed in the penicillin group with 25 percent than in the penicillin-malaria group with 15.6 percent. By the end of 18 months, 88.9-percent reversal occurred in the spinal fluids and 75-percent reversal in the blood serologic tests. The highest proportion of reversals in spinal fluid and blood serologic tests occurred in the group who had received 6 months or more of routine treatment during the previous year.

With regard to correlation between spinal fluid and blood reversal, it was shown that 50 percent of the 36 patients showing spinal fluid reversal also showed blood reversal. Of the 24 patients showing blood reversal, 75 percent showed spinal fluid reversal.

The better performance in terms of spinal fluid and blood reversal of the group receiving penicillin alone confirms the impression that penicillin alone is as effective as penicillin and malaria for most types of neurosyphilis.

Syphilitic primary optic atrophy as a cause of blindness; importance of early diagnosis. Joseph V. Klauder, George P. Meyer and Benjamin A. Gross. Am. J. Syph., Gonor. & Ven. Dis., 32: 574–586, 1948.

A review of the literature is presented, and data from other studies are presented as comparisons.

Data on 397 patients with syphilitic primary optic atrophy are presented. Of this number, 20 had congenital syphilis. Of the 377 patients with acquired syphilis. 216 were white and 161 were Negroes. Sixty-four percent had a tabetic form of neurosyphilis, 30.5 percent had diffuse meningovascular neurosyphilis, 2 percent had taboparesis, and 3.5 percent had general paresis. Of the 20 patients with congenital syphilis, 12 were white and 8 were Negroes. Fifty-five percent of this group had the tabetic form of neurosyphilis, 25 percent diffuse meningovascular neurosyphilis, 15 percent taboparesis, and 5 percent general paresis.

The predominating age group in which the patients with acquired syphilis complained of impaired vision was from 40 to 50. Males of both races were more affected than females in a ratio of 3.5 to 1. In the series of congenital syphilis patients, females predominated. Altogether, optic atrophy was observed in patients ranging in ages from 9 to 75.

Of the 377 patients in the acquired syphilis group, 309 (82 percent) were untreated in the interval between onset of loss of vision and admission to the clinic. The remaining 68 patients (18 percent). received treatment during this interval, but previous to admission to the clinic. The majority of the 377 patients had received no treatment in the early stages of the infection, and few, if any, received treatment in amounts considered adequate according to modern standards.

In addition to impaired vision as a symptom of optic atrophy, pain in the legs, diplopia, impairment of adaptation to light, and difficulty in distinguishing colors may aid in an early diagnosis. The authors believe the earliest symptom of optic atrophy preceding loss of central vision and pallor of the disc is a visual field defect. The earliest field losses in primary optic atrophy are those for color, particularly red and green. Subsequent to visual field defect, the optic disc shows some degree of pallor.

Sixty-one percent of the patients when first seen at the clinic were either industrially blind or had visual acuity of less than 1/60. To facilitate an early diagnosis, it is necessary that ophthalmologists and physicians who examine patients with syphilis have a high degree of awareness of the optic nerve. The authors estimate that 90 percent of blindness caused by syphilis can be attributed to optic atrophy of acquired and congenital syphilis.

Case histories are given on six of the patients.

Acute syphilitic meningitis. A report of 80 cases. Osvaldo A. Pardo and Thomas W. Farmer. Am. J. Syph., Gonor. & Ven. Dis., 32: 587–598, 1948.

This study was based upon 80 patients with the clinical syndrome of early acute syphilitic meningitis diagnosed at the Johns Hopkins Hospital between 1918 and 1947. Of the 80 patients, 52 were male, and 28 were female; 23 were white, and 57 were Negroes. Their ages varied from 15 to 51 years with 93 percent between the ages of 15 and 40. Sixty had a history of early syphilis, while in the remaining 20, the meningeal symptoms were the first observed clinical manifestation of the infection. Thirty of the patients had had no treatment for early syphilis, while 50 had received therapy varying from 1 to 55 arsenical injections with from 1 to 50 bismuth injections. Symptoms of acute syphilitic meningitis appeared from a few days to 16 months after lapse of treatment. The most common symptom in the entire group was headache which occurred in 66 of the patients. Nausea and vomiting were observed in 32 patients, while in 12 the temperature was elevated about 100° F. Papilledema was observed in 22 patients, 22 had definite changes in mental status which varied from confusion to coma, 44 had involvement of one or more cranial nerves, and in 11 mucocutaneous lesions were associated with the meningitis. The serologic test was positive in 56 of the 69 patients who had serologic tests performed within a few days of the time of a diagnosis of meningitis. Doubtful results were noted in 2 serums, while 11 were negative. The cerebrospinal fluid in most cases was clear and colorless. The total protein content was determined in 52 cases with results varying from 20 to 440 mg. per 100 cc. Complement-fixation tests gave positive reactions in 74 patients and a negative reaction in 6 patients.

Case histories are given for two deaths which occurred. One patient died prior to the beginning of therapy, and the other died while under treatment with neoarsphenamine. Of the remaining 78 patients, 60 were treated with heavy metals and 18 with penicillin. The rate of disappearance of signs of meningeal irritation and of increased intracranial pressure was approximately the same in patients treated with arsenical drugs as in those treated with penicillin. Headache, nausea, vomiting, fever, stiff neck, coma, and convulsions disappeared within 7 days in three-fourths of the patients in each group, and papilledema subsided within a week in the majority of patients. Late results were studied in 29 patients treated with arsenical drugs and 18 who received penicillin therapy. Similar rates of clinical improvement and response in the abnormalities of the cerebrospinal fluid and blood serologic tests were noted in both groups. One patient treated with arsenicals developed recurrent meninigitis 15 months after the onset of initial therapy, two patients treated with penicillin required re-treatment due to the recurrence of increased cell counts and total protein content in the cerebrospinal fluid, and four patients (one treated with arsenicals and three with penicillin) had recurrences of mucocutaneous lesions following treatment in small dosages.

The authors believe that penicillin in a total dosage of approximately 5,000,000 units of crystalline penicillin G over a period of 7 to 10 days is the treatment of choice in acute syphilitic meningitis at the present time and that prolonged follow-up study is required.

Vagotomy in the treatment of gastric crises of tabes dorsalis. Charles W. Stoops, Jr., Leonard S. Markson, James M. Sullivan and Joseph Kanter. Am. J. Syph., Conor. & Ven. Dis., 32: 599–603, 1948.

A review of the pathologic and therapeutic literature regarding gastric crises of tabes dorsalis is presented.

The pathologic picture in tabes is not constant and variations are numerous. The outstanding pathologic change is a degeneration of the nerve fibers of the dorsal spine roots and of the dorsal columns of the spinal cord, where the fibers are replaced by scar or glial tissue. The motor symptom of gastric crises is vomiting. Alleviation of the nausea and vomiting in protracted cases of gastric crises in tabes dorsalis has always been a difficult therapeutic problem.

Four patients were selected for surgical supradiaphragmatic vagotomy who had had various types of medical treatment without relief. Case histories of these four are presented. One of the patients had a history of chancre and secondary syphilis, one of chancre and gonorrhea, one of chancre, and the other with no history of a lesion or secondary syphilis.

The operation did not relieve the pain in any patient, but it did stop the vomiting in three and lessened its occurrence in the other patient. Reexamination of the patients approximately a year later shows that two of them have maintained their improvement as far as vomiting is concerned, but the other two were classed as failures both as to vomiting and pain.

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CURRENT NOTES AND REPORTS

The Prevalence of Syphilis in Pregnant Women in Athens, Greece, From 1935 to 1940

D. A. Messinezy, M. D., M. P. H.[1]

In order to estimate the prevalence of syphilis (*1*) and as a preventive measure, routine serologic tests have been performed at the prenatal clinic of the Ambelokipi Health Centre (*2*) since 1935. From 1935 to 1937, the Sachs-Georgi (citochol reaction) and Wassermann tests were used; from 1937 to 1940, the Wassermann and Kahn tests were employed. All serologic tests were carried out at the Evanghelismos Hospital Laboratories.

During the 5-year period, 1,133 tests were performed in 1,498 pregnancies, which represented approximately half the pregnancies recorded in the entire Ambelokipi District. Of these recorded pregnancies, half were admitted before the last trimester of pregnancy. Serologic tests during this period showed 2.5 percent positive (ranging, by years, from 1 percent to 3.2 percent) and 0.4 percent doubtful reactions.

Routine serologic examinations were started similarly in 1937 at the large cooperating Marika Eliadou Maternity Hospital. Pangalos and Kyriakis (*3*) reported 1.5 percent positive and 1 percent doubtful findings in a series of 4,000 pregnancies, including an initial 700 pregnancies examined at the Ambelokipi Health Centre. By excluding these 700 cases, the percentage of positives was found to be 1.1 percent, whereas the percentage of doubtful cases remained at 1 percent. The serologic examinations were performed at the Marika Eliadou Laboratory.

The difference observed between the results of the Ambelokipi Health Centre examinations and those made at the Marika Eliadou Maternity Hospital was significant,[2] and may be due to factors in which the two series differed, such as laboratory technics or attendance earlier in pregnancy at the Ambelokipi Health Centre. On the other hand, it is possible that there is an essential difference between the two series. For example, the Marika Eliadou Maternity Hospital cases were drawn from the entire city of Athens and surrounding areas, whereas the Ambelokipi Health Centre cases came from a confined district of the city having a high proportion of displaced persons living under poor conditions.

Summary

Routine serodiagnostic tests for syphilis in pregnancy, performed in Athens—most densely populated and highly industrialized urban center of Greece—showed a positive rate of 2.5 percent in one section of the city having poor living conditions as compared to a positive rate of 1.1 percent in another series of cases drawn from the wider population of greater Athens.

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3. Pangalos and Kyriakis: The serodiagnosis of syphilis during pregnancy. Observations and conclusions. Iatrike Athine. February 25, 1939. (In Greek.)

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[1] Formerly Medical Director, Ambelokipi Health Centre, Athens, Greece; now Medical Officer, World Health Organization, Geneva, Switzerland.

[2] The observed difference exceeds twice its standard error:

$$\frac{-P\times Q}{N}+\frac{P\times Q}{N}=0.5$$

STATISTICS

Cases of Syphilis and Gonorrhea Reported to the Public Health Service by State and Territorial Health Departments, Second Quarter Fiscal 1949

[Known military cases excluded]

Federal Security Agency regions	Syphilis															Gonorrhea		
	Primary and secondary			Early latent			Late and late latent			Congenital			Not stated					
	Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter	
		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources
Region 1—Total	324	1. 27	1. 30	172	0. 86	1. 03	597	0. 94	1. 08	63	1. 00	0. 90	129	1. 18	1. 06	1, 136	0. 84	0. 69
Connecticut	58	1. 76	(b)	66	. 86	. 93	125	1. 01	1. 11	8	(b)	(b)	49	1. 32	(b)	232	. 77	. 76
Maine	74	1. 19	1. 08	23	(b)	(b)	62	1. 19	(b)	5	(b)	(b)	6	(b)	(b)	82	. 86	. 78
Massachusetts	126	1. 15	1. 32	49	. 73	(b)	266	. 90	1. 04	34	1. 13	(b)	0	(c)	(c)	645	. 90	. 58
New Hampshire	18	(b)	(b)	9	(b)	(b)	33	(b)	(b)	4	(b)	(b)	1	(b)	(b)	42	. 79	. 89
Rhode Island	28	(b)	(b)	24	(b)	(b)	98	. 72	. 78	3	(b)	(b)	39	1. 03	(b)	70	. 75	. 91
Vermont	20	(b)	(b)	1	(b)	(b)	13	(b)	(b)	9	(b)	(b)	34	1. 13	(b)	65	. 66	. 66
Region 2—Total	2, 009	1. 09	1. 35	3, 473	1. 02	1. 14	6, 546	1. 06	. 96	346	. 94	1. 02	209	1. 10	1. 14	11, 291	. 95	1. 03
Delaware	58	1. 57	(b)	72	. 86	1. 08	57	1. 73	(b)	7	(b)	(c)	57	1. 21	(b)	44	. 51	. 51
New Jersey	249	. 82	. 90	626	. 69	. 94	906	. 79	. 85	42	. 86	(b)	43	(b)	(b)	1, 156	. 76	. 92
New York	1, 198	1. 22	1. 48	1, 582	1. 19	1. 28	4. 428	1. 08	. 98	190	1. 06	1. 11	69	. 81	. 71	7, 682	1. 01	1. 07
New York City	994	1. 27	1. 75	1, 479	1. 23	1. 32	3, 421	1. 12	. 99	134	1. 01	1. 04	56	. 86	(b)	6, 154	1. 02	1. 22
Pennsylvania	504	. 96	1. 30	1, 193	1. 09	1. 15	1, 155	1. 25	1. 11	107	. 78	(b)	40	1. 05	(b)	2, 409	. 92	(c)
Philadelphia [a]	224	1. 05	(c)	806	. 99	(c)	681	1. 32	(c)	36	. 75	(c)	5	(b)	(c)	2, 262	. 95	(c)
Pittsburgh [a]	115	. 91	(c)	100	. 82	(c)	155	. 92	(c)	17	(b)	(c)	0	(c)	(c)	238	. 78	(c)
Region 3—Total	2, 019	. 86	. 91	2, 391	. 90	. 90	2, 197	. 85	. 85	255	. 79	1. 38	62	. 77	(b)	13, 615	. 85	. 82
District of Columbia	253	1. 03	(b)	291	. 81	. 82	379	. 87	. 68	31	(b)	(b)	0	(c)	(c)	4, 192	. 81	. 77
Maryland	461	1. 05	. 97	466	. 97	. 74	632	. 89	. 85	70	. 88	(b)	32	. 76	(b)	1, 748	. 81	. 88
Baltimore	259	. 98	(b)	273	. 80	. 53	443	. 80	. 64	39	. 76	0	29	. 72	(b)	1, 326	. 79	. 83
North Carolina	560	. 76	. 85	689	. 96	. 84	281	. 98	1. 11	71	. 76	(b)	0	(c)	(c)	3, 773	. 91	1. 20
Virginia	403	. 73	. 89	579	. 74	. 82	440	. 74	. 71	42	. 60	(b)	30	. 77	(b)	2, 786	. 85	. 90
West Virginia	342	. 94	. 93	366	1. 10	1. 10	465	. 85	. 94	41	. 75	(b)	0	(c)	(c)	1, 116	. 90	. 73
Region 4—Total	1, 407	. 84	. 75	2, 498	. 92	. 89	4, 271	. 92	. 87	338	. 91	. 89	266	. 60	. 60	6, 960	. 96	1. 14
Kentucky	237	. 65	. 61	305	. 90	1. 06	491	1. 00	1. 01	44	1. 05	(b)	10	(b)	(b)	1, 447	. 81	. 68
Michigan	483	. 99	. 89	533	. 96	1. 14	1, 252	. 93	. 93	122	1. 13	. 83	256	. 59	. 60	2, 288	. 88	. 82
Ohio	687	. 84	. 71	1, 660	. 91	. 83	2, 528	. 90	. 83	172	. 78	. 87	0	(c)	(c)	3, 225	1. 13	1. 85
Region 5—Total	1, 316	1. 06	1. 06	1, 725	1. 10	1. 26	2, 880	1. 09	1. 14	257	. 98	1. 14	2	(b)	(b)	8, 091	. 90	1. 04
Illinois	858	1. 02	1. 00	1, 185	. 99	1. 07	1, 899	1. 08	1. 14	115	. 85	. 96	0	(c)	(c)	6. 797	. 89	1. 06
Chicago	546	1. 04	1. 07	849	1. 01	1. 16	1, 056	1. 06	1. 12	67	. 92	(b)	0	(c)	(c)	5, 294	. 86	1. 02
Indiana	339	1. 16	1. 28	406	1. 72	3. 22	664	1. 44	1. 75	118	1. 30	(b)	0	0	0	768	1. 00	1. 20
Minnesota	37	. 84	. 71	33	. 85	(b)	116	. 87	. 77	7	(b)	(b)	2	(b)	(b)	309	. 95	. 87
Wisconsin	82	1. 15	1. 21	101	1. 11	. 90	201	. 73	. 72	17	. 57	(b)	0	(c)	(c)	217	. 80	. 84

Region 6—Total	3,670	.77	.95	5,798	.83	1.13	4,937	.83	1.19	1,146	1.01	1.08	823	.84	.86	20,996	.86	1.32
Alabama	572	.81	.73	710	.42	.42	450	.39	.55	62	.57	(b)	773	.84	.85	1,235	.73	.74
Florida	953	.90	1.13	1,468	1.21	1.54	1,589	1.38	1.73	170	.96	1.61	0	0	(c)	4,166	.99	2.87
Georgia	689	.74	.86	845	1.07	(c)	800	1.03	1.07	268	1.62	(c)	26	(b)	(c)	3.526	.79	(c)
Mississippi	494	.72	2.05	745	.77	1.88	964	.64	1.55	146	.67	(b)	0	(c)	(c)	2.308	.82	1.16
South Carolina	474	.67	.69	713	.96	.82	324	.91	.56	51	.69	(c)	0	(a)	(c)	2.318	.98	(c)
Tennessee	347	.64	.88	483	.78	.93	443	.75	.90	62	.83	(b)	19	(b)	(b)	5,295	.86	1.13
Puerto Rico	129	.83	(c)	813	.89	(c)	322	.84	(c)	380	1.23	(c)	1	(c)	(c)	2,109	.76	(c)
Virgin Islands	12	(b)	(c)	21	(b)	(c)	15	(b)	(c)	7	(b)	(c)	4	(b)	(c)	39	(b)	(c)
Region 7—Total	714	.96	1.14	915	1.10	1.26	1,512	1.11	1.22	134	.95	.99	136	1.20	1.34	2,415	.82	.85
Iowa	128	1.31	1.25	99	1.05	1.05	167	1.15	1.06	16	(b)	(b)	0	(c)	(c)	259	.69	.68
Kansas	155	1.17	1.30	208	1.28	1.48	567	1.39	1.32	49	1.17	(b)	0	(c)	(c)	328	.72	.86
Missouri	328	.81	1.10	500	1.07	1.38	640	.97	1.29	55	.93	(b)	70	1.30	1.46	1,458	.87	.96
St. Louis	138	.77	1.20	292	1.23	2.26	345	1.04	1.51	16	(b)	(b)	0	(c)	(c)	900	.85	.67
Nebraska	35	.70	(b)	57	.90	.79	99	1.01	1.01	7	(b)	(b)	51	.86	.96	201	.96	1.05
North Dakota	24	(b)	(b)	16	(b)	(b)	14	(b)	(b)	1	(b)	(b)	15	(c)	(c)	71	1.18	1.18
South Dakota	44	1.42	(b)	35	.95	(b)	25	(b)	(b)	6	(b)	(b)	0	(c)	(c)	98	.66	.63
Region 8—Total	1,838	.81	.73	2,763	.78	.60	3,496	.72	.86	727	.77	.62	1,607	.64	.62	11,645	.82	.93
Arkansas	277	.71	.55	626	.55	.43	1.416	.56	.73	277	.82	.74	3	(c)	(b)	1,067	.72	.94
Louisiana	444	.71	(b)	578	.80	(b)	606	.93	(b)	94	.66	(b)	370	.82	.98	2,582	.71	1.13
New Mexico	65	1.20	(b)	118	1.11	(b)	112	.97	(b)	22	(b)	(b)	0	(c)	(c)	259	.86	.95
Oklahoma	262	.90	.79	308	.82	.83	520	.78	.84	55	.59	.59	48	1.14	.91	1.527	.82	.93
Texas	790	.86	.97	1,133	.94	1.22	842	.97	1.40	279	.82	(b)	1,186	.59	.59	6.210	.89	.93
Region 9—Total	171	.81	.88	175	.98	.80	294	.97	1.05	41	1.02	(b)	21	(b)	(b)	776	.82	1.29
Colorado	72	.66	.76	67	.86	.67	105	.88	.89	10	(b)	(b)	0	(c)	(c)	471	.81	1.32
Idaho	15	(b)	(b)	15	(b)	(b)	38	.79	(b)	2	(b)	0	16	(b)	(b)	100	.62	(b)
Montana	43	.98	(b)	43	1.08	(b)	52	.87	1.00	8	(b)	(b)	0	0	0	51	.57	.67
Utah	30	(b)	(b)	33	(b)	(b)	74	1.68	(b)	21	(b)	(b)	0	(c)	(c)	101	1.22	(b)
Wyoming	11	(b)	(b)	17	.57	(b)	25	.81	(b)	0	0	0	5	(b)	(b)	53	1.71	(b)
Region 10—Total	1,060	.94	.89	1,155	.77	.76	2.380	.86	.81	192	.77	.82	267	.99	1.30	8,104	.91	.90
Arizona	75	1.15	(b)	99	.93	(b)	86	.91	(b)	13	(b)	(b)	0	(c)	(c)	217	.83	.72
California	807	.99	.92	812	.68	.61	1,833	.83	.77	130	.79	.81	209	.91	.77	6.326	.91	.91
Nevada	24	(b)	(b)	35	(c)	(c)	110	1.03	1.05	12	(b)	(b)	0	(c)	(c)	239	1.34	1.44
Oregon	57	.78	(b)	47	1.27	(b)	83	.78	.78	2	(b)	(b)	0	(c)	(c)	284	.87	.63
Washington	83	.70	.71	100	.80	(b)	194	.97	1.02	20	(b)	(b)	34	(b)	(b)	728	.95	95
Alaska	9	(b)	(b)	42	(b)	(b)	38	(b)	(b)	6	(b)	(b)	21	(b)	(b)	130	1.06	1.06
Hawaii	5	(b)	(b)	20	(b)	(b)	36	.64	(b)	9	.30	(b)	3	(b)	(b)	180	.73	.67
Canal Zone	1	(b)	(c)	17	(b)	(c)	24	.49	(c)	1	(b)	(c)	6	(c)	(c)	161	.94	(c)
Continental United States	14,373	.88	.97	20,169	.89	.98	28,669	.91	.98	3,097	.88	.95	3,493	.74	.72	82.571	.88	.98
Total United States including Territories	14,529	.88	.97	21,082	.89	.99	29,104	.91	.98	3,500	.90	.95	3,528	.75	.72	85.190	.88	.98

[a] Data from VM-820.
[b] Rate not calculated, base is less than 30.
[c] Rate not calculable, base is zero or unknown.

Source: Form 8958-B FSA—PHS—Division of Venereal Disease, Office of Statistics, 3/17/49 (ML-MJM) as.

Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in THE JOURNAL OF VENEREAL DISEASE INFORMATION, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the JOURNAL, and should be presented on separate sheets, rather than within text material.

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Chief, Division of Venereal Disease

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Editorial

A year ago we launched an experiment to discover whether radio could be used successfully as a venereal disease case-finding instrument. Two major questions had to be answered: (1) Can we tell the venereal disease story on the air without offense? (2) Can we tell it in such a way as to persuade those who suspect infection to seek diagnosis? The answer to both of these questions is "yes."

In the spring and summer of 1948, a series of 14 transcribed radio programs was produced in cooperation with Columbia University. These dramatic, musical, and documentary programs starred some of the biggest names in the radio and moving picture fields and gave a direct, hard-hitting venereal disease message. Since August 1948, when they were first released, these programs have been aired over some 135 commercial stations in about 85 communities throughout the United States. They have also been broadcast to Europe over Voice of America and to 10 other countries.

Communities have used the programs in conjunction with local case-finding campaigns. Although it is impossible to separate the effect of specific radio programs from those of other public appeal mediums, reports from areas using the broadcasts show a large increase in the number of persons seeking diagnosis.

On the basis of the effectiveness of public appeal channels in telling the VD story, July and August will find public health officials throughout the Nation embarking on a simultaneous effort to find cases with every means at their disposal. Already such campaigns are being planned in over 200 communities. The major radio networks and magazines are planning to reinforce local efforts. This carries out the recommendation of Surgeon General Scheele, who, before a television audience last fall, suggested that every city in the country should consider the possibility of a venereal disease public appeal case-finding campaign such as that then being conducted in New York City.

The Public Health Service is providing funds and assistance for such campaigns. The purchase and use of public appeal materials and the production of effective materials are being encouraged from a variety of sources, particularly the new Columbia University Communication Materials Center, which is described on page 174 of this issue.

The most successful campaign results are obtained in those communities where effective public appeal goes hand in hand with energetic contact investigation. Public appeal alone can find a certain number of cases, but without speedy and thorough contact investigation a great part of the public appeal effort is wasted.

Stimulating Venereal Disease Morbidity Reporting by Private Physicians

I. Follow-up of Positive Serologic Test Reports

Benson H. Sklar, A. B., M. Sc. P. H.,[1] and Leonard M. Schuman, M. D., M. Sc.[2]

The reporting of all known cases of venereal disease is of prime importance in the development of an adequate venereal disease control program. Such a program must give consideration to the extent of the venereal disease problem expressed numerically and geographically for the jurisdiction of the health agency promoting the program. Focusing attention upon this need, the Division of Venereal Disease Control of the Illinois State Department of Public Health has used several procedures to stimulate the reporting of venereal diseases by private physicians, clinics, and public institutions.

At the present time, all cases coming to the 30 venereal disease clinics maintained by the Illinois State Department of Public Health are reported to the Division of Venereal Disease Control on specially designed venereal disease morbidity cards,[3] while all venereal disease cases in institutions under the jurisdiction of the Illinois Departments of Public Welfare and of Public Safety are reported on regular morbidity report forms. It is, therefore, the reporting of venereal disease cases by private physicians which requires greater stimulation in order to determine as completely as possible the extent of the venereal disease problem in Illinois.

With this aim in mind, the Division of Venereal Disease Control developed special procedures designed to stimulate the reporting of venereal disease by private physicians. This first paper will deal with the follow-up of positive venereal disease laboratory reports as one important device toward this end. Only serologic tests for syphilis are considered in this analysis, although a procedure similar to that outlined below is being applied to reports on smears for gonorrhea.

Method

On January 1, 1944, a system of following up positive laboratory reports was devised which utilizes the central registry of cases and contacts in the Division of Venereal Disease Control. This registry, composed of I. B. M. punch cards filed alphabetically by name of case or contact, contains not only morbidity data, but also treatment and laboratory information, results of investigations, mortality data, and correspondence references, as well as selectee and separatee reports.

In this follow-up system, positive laboratory reports for syphilis received in the Division of Venereal Disease Control are checked against the central registry files in order to determine if corresponding morbidity reports from private physicians have been received. This check is not made until 21 days[4] after receipt of laboratory reports, in order to allow the private physician ample time to make a definite diagnosis before sending a morbidity report to the Division of Venereal Disease Control. If no morbidity report has been received by the time this check is made, the Division of Venereal Disease Control sends the following letter to the private physician:

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[1] Administrative Assistant, Division of Venereal Disease Control, Illinois State Department of Public Health.

[2] Chief, Division of Venereal Disease Control, Illinois State Department of Public Health.

[3] U. S. Public Health Service Budget Bureau No. 68–4–100.

[4] Prior to July 1, 1947, a preliminary check was made upon receipt of the laboratory reports, followed by another check 14 days later.

Dear Doctor:

The Division of Laboratories has reported that the specimen of blood submitted from____________________________
is positive.

If a diagnosis of syphilis has been made, will you kindly report this case on regular physician's venereal disease report form in accordance with the State law requiring all such cases to be reported?

If you have already reported this case, please state below the venereal disease report number and date.

Your cooperation in this matter will be greatly appreciated.

Very truly yours,
_____ ______.

If such letters are not answered within a second 21-day interval [5] by either a morbidity report or by an explanation concerning the disposition of the positive report, such as "false positive," "unable to locate," or "died," an assignment is sent to the district health department in whose jurisdiction the private physician practices to obtain a morbidity report from the private physician if his patient has been diagnosed as having a venereal disease. During an interview with the physician, the health department employee offers to send drugs for the treatment of the patient, to follow up delinquent patients, and to interview the contacts of possibly infectious cases. Although the purpose of the interview is to obtain the morbidity report, the offer of services is the entree to the physician.

Results

The above procedures have resulted in securing a high percentage of morbidity reports which otherwise might never have been obtained. A check was made in 1947 to determine the effectiveness of these procedures by analyzing a 3 months' sample of positive blood tests for syphilis, taken from laboratory records of the previous year 1946. The analysis showed that, of the 1,688 positive blood tests in the sample, 1,057 (62.6 percent) had been reported by the private physician as cases of syphilis without need for follow-up (table 1). Letters to private physicians requesting reports and subsequent assignments, when necessary, to district health units to follow up the remaining 631 positive blood test reports with no corresponding morbidity reports in the central registry yielded 324 (51.3 percent) additional syphilis morbidity reports; this represented an increase of 19.2 percent in the number of morbidity reports filed in the central registry by private physicians. Of these, 115 (35.5 percent) were cases of early syphilis. Thus, of the 1,688 laboratory reports, 1,381 (81.8 percent) were eventually reported as cases of syphilis to the central registry.

It was on the basis of this sample analysis that clerical procedures were changed to give the private physician a longer period of time for diagnosis before requesting a morbidity report from him. It was also decided that a more comprehensive study be made to evaluate this change.

A tabulation was therefore made of the results of checking positive blood tests received for patients of private physicians in district health jurisdictions against the central registry files during the period July 1, 1947, through June 30, 1948, and of the follow-up of cases for which there was no morbidity report from the private physician (table 2). In this period, 6,611 positive blood test reports received from State laboratories were checked with the central registry files for corresponding morbidity reports from private physicians (table 2). This check against the central registry files, made 21 days after the receipt of each positive laboratory report, indicated that 4,516 corresponding syphilis morbidity reports (68.3 percent) had already been filed by private physicians. Of this number, 2,051 (45.4 percent of the morbidity reports received) were in the infectious or potentially infectious stage (table 3). Letters were then sent to private physicians requesting morbidity reports for the remaining 2,095 positive blood test reports for which no corresponding morbidity reports could be found. These

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[5] Prior to July 1, 1947, the interval was 14 days.

Table 1.—*Results of follow-up of positive blood tests for syphilis to obtain morbidity reports from private physicians in Illinois*

	Fiscal year 1948		3 months, 1946	
	Number	Percent	Number	Percent
Total positive blood-test reports for syphilis received from State laboratories	6, 611	100. 0	1, 688	100. 0
Morbidity reports in central registry at time of initial check	4, 516	68. 3	1, 057	62. 6
Results of follow-up with private physicians for missing reports:				
Additional morbidity reports obtained	1, 793	27. 1	324	19. 2
Morbidity reports not obtained	302	4. 6	307	18. 2
False positives	83	1. 3	----------	----------
Cases not located [1]	102	1. 6	----------	----------
Reports claimed but not found [2]	28	. 4	----------	----------
No response from physician	89	1. 3	----------	----------

[1] Patient left physician's care before diagnosis could be established.

[2] Physician's reply indicated report submitted, but report not found in central registry.

letters and subsequent follow-up assignments to district health departments yielded 1,793 new reports of syphilis (85.6 percent of the total formerly unreported) (table 4), representing an increase of 27.1 percent of morbidity reports from private physicians in the central registry (table 1). Of these, 701 (39.1 percent of the new morbidity reports) were cases of early syphilis (table 5).

Thus, of the 6,611 laboratory reports, 6,309 (95.4 percent) were eventually reported as cases of syphilis in the central registry (table 1). The remaining 4.6 percent represented false positives (1.3 percent), individuals who failed to reappear for further diagnostic tests (1.6 percent), individuals for whom private physicians insisted reports had been forwarded (0.4 percent), and no response (1.3 percent). This last category, a very small percentage of the total number of

Table 2.—*Morbidity reports found on initial check in central registry in Illinois, fiscal year 1948*

	Number	Percent
Total positive serology test reports received from State laboratories	6, 611	100. 0
Corresponding morbidity reports from private physicians found in central registry on initial check	4, 516	68. 3
Corresponding morbidity reports from private physicians not found in central registry on initial check	2, 095	31. 7

Table 3.—*Stage of syphilis reported by private physicians in Illinois in morbidity reports received without need for follow-up, fiscal year 1948*

	Number	Percent
Total morbidity reports found on initial check	4, 516	100. 0
Stage of syphilis reported:		
Early syphilis	2, 051	45. 4
Primary	422	9. 3
Secondary	628	13. 9
Early latent	1, 001	22. 2
Late and late latent	2, 256	50. 0
Congenital	209	4. 6

Table 4.—*Morbidity reports submitted to central registry in Illinois after follow-up, fiscal year 1948*

	Number	Percent
Total positive serologic test reports for which follow-up was necessary	2, 095	100. 0
Morbidity reports obtained from private physicians after follow-up	1, 793	85. 6
False positives	83	4. 0
Cases not located [1]	102	4. 9
Reports claimed but not found [2]	28	1. 3
No response from physician	89	4. 2

[1] Patient left physician's care before diagnosis could be established.

[2] Physician's reply indicated report submitted, but report not found in central registry.

Table 5.—*Stage of syphilis reported by private physicians in Illinois in morbidity reports received as a result of follow-up, fiscal year 1948*

	Number	Percent
Total morbidity reports received after follow-up	1,793	100.0
Stage of syphilis reported:		
Early syphilis	701	39.1
Primary	156	8.7
Secondary	205	11.4
Early latent	340	19.0
Late and late latent	1,035	57.7
Congenital	57	3.2

positive laboratory reports, indicates the degree of noncooperation by private physicians.

Table 1 contrasts the data of the 1946 sample with the analysis of the complete fiscal year 1948.

Discussion

It is apparent from the results of this study that morbidity reports were submitted without need for follow-up for two-thirds of all positive serologic tests made for private physicians, as evidenced by the initial check of the central registry. Although this may be assumed to represent spontaneous reporting by the private physician, it must be remembered that an undetermined proportion of this represents the results of stimulation in the earlier years of the procedure. Furthermore, an undetermined portion may be due to requests for such a morbidity report when the physician requisitioned drugs. Since the positive laboratory test would reach the Division of Venereal Disease Control prior to the physician's decision to request such drugs, the number of instances in which a morbidity report would be received as a result of such a request would be small and would occur only if the initial serodiagnostic tests were performed in a private laboratory.

Comparing the data of the 3 months' sample of 1946 with that for the fiscal year 1948 (table 1), a statistically significant difference (5.7±1.3 percent)[6] is noted in the percentage of morbidity reports found in the central registry on the initial check. This improvement may well be the result of the increased waiting period (from 14 to 21 days) in the fiscal year 1948, which allowed the physician an additional 7 days in which to establish and to report a diagnosis. Probably a longer interval might have resulted in the finding of a greater number of morbidity reports on the initial check, but the interval in use was accepted as a compromise between that employed prior to July 1947 (possibly too short a time for the establishment of a diagnosis of latent syphilis) and any period beyond 21 days (when the advantage to be gained through early contact investigation might be lost).

Letters to private physicians requesting morbidity reports and assignments to field workers encouraging such morbidity reporting resulted in 85.6 percent success in the fiscal year 1948, as compared to 51.3 percent in the 3 months' sample of 1946. This remarkable improvement is statistically significant (34.3±1.9 percent),[6] and may be explained by several factors which, in this study, could not be controlled. The prolongation of the interval between the letter to the physician and the assignment to the district health department may well have permitted the establishment of the diagnosis by the time personal contact was made with the physician. Certainly, the increasing acquaintance of physicians with the system as well as the increasing recognition of its importance by health department workers, has played no small part in this increase.

The surprisingly small percentage (1.3 percent) of instances in which the physician refused to cooperate reflects in great part the rapport which has been established in venereal disease control activities. It must be remembered that the entree to requesting morbidity reports after form letters have failed is predicated on the service which the district health department can give to the private physician. Practitioners who have received free drugs from the State for their previous cases, who have had their delinquent early cases brought back to treatment, who have had their technical questions on diagnosis and treatment answered, and for whom arrangements have been made for the treatment of medically indigent patients are willing to supply morbidity reports. The initial failure of the physician to make the report is generally attributed to an "oversight."

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[6] Standard error of the difference between two proportions $= \sqrt{\frac{pq}{n_1}+\frac{pq}{n_2}}$

It is apparent from the results of this study that the follow-up of positive laboratory test reports for syphilis yields a highly significant increase in the number of morbidity reports from private physicians in the central registry. It has already been mentioned that such morbidity reporting is the point of departure in organizing and maintaining venereal disease control programs. When one considers that over 25 percent more reports may be obtained by such a system of follow-up and that approximately 40 percent of these new reports represent early infectious and potentially infectious syphilis, the value of such a follow-up procedure may be appreciated.

Summary

1. This study of the value of a procedure to follow up positive serologic test reports for syphilis made by private physicians for which no corresponding morbidity reports were received comprises a 3 months' sample involving 1,688 positive reports, as well as a full year's analysis of 6,611 reports of positive tests.

2. The success of the follow-up procedure in our hands is indicated by the fact that 95.4 percent of the positive test reports in the fiscal year 1948 yielded corresponding morbidity reports.

3. The value of prolonging the initial checking period from 14 to 21 days is shown by an increase of 5.7 percent in the morbidity reports found on the initial check in the central registry.

4. The value of prolonging the interval between sending a form letter to the physician and assigning failures to the district health department for the follow-up of the case with the physician is inferred.

5. The application of the follow-up system to cases unreported at the time of the initial check led to 85.6 percent success in the fiscal year 1948 in obtaining new case reports, 39.1 percent of which were cases in the primary, secondary, and early latent stages of the disease, a percentage which is highly important for further contact tracing.

6. The high degree of cooperation (98.7 percent) by private physicians in this system in the fiscal year 1948 is described and the reasons for the small degree of failure to obtain a morbidity report (4.6 percent) are analyzed; replies were lacking from only 1.3 percent of the physicians.

Syphilis Contact Investigation in a Rural County in Mississippi

A. L. Gray, M. D.;[1] Albert P. Iskrant, Principal Statistician;[2] and Richard S. Hibbets, Health Program Representative[2]

Introduction

A previous report (*1*) described the planning, operation, and results of a venereal disease case-finding project carried out in Quitman County, Miss., during the period September 1, 1947, through June 30, 1948. The project demonstrated the effectiveness of a case-finding program which included contact investigation, intensive venereal disease education, and screen blood testing.

This paper is devoted in the main part to the contact investigation phase of the project. The statistical data are based on the records of primary and secondary syphilis patients and their contacts who were brought to treatment in Quitman County during the project period.

The project organization consisted of seven persons: a project director (nurse), a clinician (doctor), a clinician's assistant (nurse), a clerk, and three venereal disease investigators. The project director was the administrative head of the group and was responsible to the Director of the Division of Preventable Disease Control of the Mississippi State Board of Health.

The three venereal disease investigators performed all the functions connected with interviewing contacts, locating contacts, and disseminating information. A careful selection of applicants was made in order to insure obtaining men of high caliber—men who were qualified from the standpoints of intelligence and education, and whose personalities were especially suited to this multiple endeavor. The investigators employed were in their middle twenties; each had completed a minimum of 2 years of college, in addition to having varied experience in supervision and training of personnel and/or sales and teaching.

We feel that much of the success of the program was due to the thoroughness with which these three investigators were trained. Immediately after being employed they were assigned to a rapid treatment center to receive training in the medical aspects of venereal disease control, contact interviewing, and venereal disease education, followed by 2 weeks' attendance at the school for newly employed investigators conducted by the Mississippi State Board of Health. This training was followed by assignment to county health department units for field work with experienced investigators. A short time later, the new investigators were sent to the United States Public Health Service Medical Center at Hot Springs, Ark., for the special 3-day contact investigation training course given under the direction of Dr. George Parkhurst.

When the project opened, eight venereal disease diagnostic clinic locations were established. Meetings were so arranged that two investigators could be working in the field while the third attended the clinic in operation at the time. All persons tentatively diagnosed by the project clinician as having primary or secondary syphilis were interviewed by the investigators; those patients who elected to take treatment at the rapid treatment center were reinterviewed at the center immediately after their diagnosis was confirmed. In both instances an epidemiologic report was made on each contact named. All such reports on Quitman County project patients, whether interviewed by the project investigator or at the rapid treatment center, were stamped "Quitman County Project." Duplication of forms was prevented by having the project investigator indicate contacts obtained by him on the patient's rapid treatment center referral record, a copy of which was supplied to the rapid treatment center interviewer. One copy of the epidemiologic report was sent to the Mississippi State Board of Health at Jackson; the other two copies were retained by the investigator until disposition was obtained on the suspect. In the event that the form had been made up at the rapid treatment center, one copy was routed to Jackson and the other was sent to the project. In cases which were out of Quitman County jurisdiction, forms were sent to Jackson for routing. When a disposition was determined, the second copy of the epidemiologic form was sent to the Jackson office, while the third copy was retained by the county health department. The high degree of cooperation maintained at all times between the interviewers at the rapid treatment centers and the project team did much to further the success of the project.

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[1] Director, Division of Preventable Disease Control, Mississippi State Board of Health.

[2] U. S. Public Health Service.

Distribution of Contacts Reported

Data regarding the contacts reported by patients diagnosed as having primary or secondary syphilis are presented below.

Patients diagnosed as having primary or secondary syphilis	*Contacts reported per patient*
0	0
12	1
23	2
15	3
13	4
8	5
8	6
7	7
1	8
1	9
0	10
1	11
89	

Every patient gave the name of at least 1 contact; however, only 12 patients named only 1 contact. The data are plotted in the form of a frequency distribution (fig. 1). The curve is necessarily skewed to the right, since it is possible to name large numbers of contacts but impossible to give fewer than "no contacts." One patient named 8 contacts, one named 9 contacts, and one named 11. Although the number of cases is extremely small, a freehand curve is drawn through the points to indicate the possible nature of the real distribution. The average or arithmetic mean, which is 3.60, may not be a good descriptive average for this purpose because of the skewed nature of the curve. The median, or middle point of the array, is 3.13, and the mode is 2, which means that more patients reported 2 contacts than any other number.

Results of Contact Investigation of Primary and Secondary Syphilis

In table 1 the available data are analyzed, including the calculation of indices as recommended by the Division of Venereal Disease of the United States Public Health Service (2). The contact index is limited to persons who are considered as being in the sexual chain of infection and does not include the children of infected parents; however, 8 children are included—the playmates who were considered contacts of a child with primary syphilis. It is noted that 268 of the 320 contacts (84 percent) were examined or their record identified. Much of the success of this project was due to the careful follow-up investigation of the contacts named, all contacts of primary and secondary syphilis patients being followed for a 90-day period from the date of their exposure.

Every effort was made to shorten the interval between the time the contact was named and the time of initial examination. To facilitate more rapid investigation, epidemiologic information obtained by the interviewer was telephoned immediately to the project headquarters from

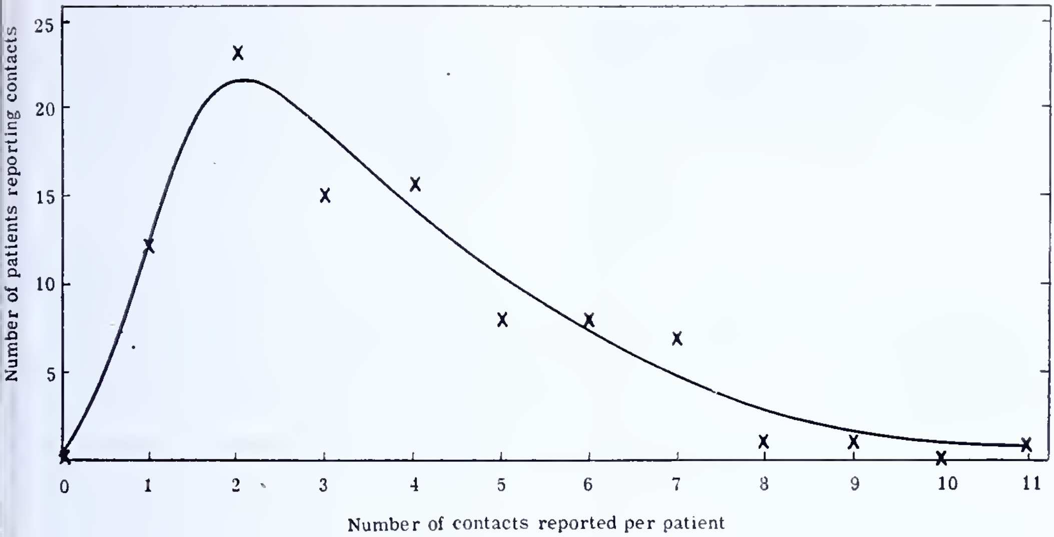

FIGURE 1.

Table 1.—*Results of contact investigation of primary and secondary syphilis cases in Quitman County, Mississippi, Sept. 1, 1947, to June 30, 1948* [1]

	Number	Index
Primary and secondary cases diagnosed by health department	89	------
Sex contacts elicited from those cases [2]	320	------
Contact index (320/89)	------	3.595
Disposition of contacts:		
No disposition or unclassified	20	------
Not located	32	------
Located and examined or record identified	268	------
Not infected with syphilis [3]	124	------
Infected with syphilis	144	------
Epidemiologic index (144/89)	------	1.618
Previously treated	72	------
Brought to treatment as a result of this investigation	72	------
Brought-to-treatment index (72/89)	------	0.809
Diagnosed in stage later than primary or secondary	36	------
Diagnosed as primary or secondary	36	------
Lesion-to-lesion index (36/89)	------	0.404

[1] 5 primary and secondary cases treated by private physicians are not included in the analysis of this project.
[2] Excludes 17 children not in the chain of infection.
[3] Includes 5 gonorrhea and 2 chancroid infections.

the rapid treatment center. All epidemiologic investigation was coordinated at the project headquarters, located in the center of the project area in the town of Marks. From these headquarters, assignments were made to investigators on the basis of the three investigation areas into which Quitman County was divided. This plan proved to be effective, since it promoted investigative efficiency and project economy.

Comparison of Quitman County Data with Published Data

A comparison of the indices and percentages calculated from the Quitman County data with those published by the Division of Venereal Disease of the United States Public Health Service for 26 areas throughout the country (*3*) reveals that the contacts obtained per patient in the Quitman County project not only were greater in number but also were more productive (table 2). The efficiency of investigation evidently matched that of interviewing in this project.

Critical Analysis of the Project

Even though the epidemiologic index exceeded 1.0 and even though the brought-to-treatment index approached 1, we were not satisfied with a lesion-to-lesion index of 0.40. We therefore went back over our records in an attempt to see where we had fallen down on the job and where we had allowed infectious cases to slip through our fingers.

Table 2.—*Comparison of contact investigation in Quitman County, Mississippi, with the average accomplishment in health departments*

	Quitman County	Average for 1947 of 26 areas having data
Number of primary and secondary syphilis cases diagnosed	89	35,174
Contact index	3.60	2.13
Epidemiologic index	1.62	.64
Brought-to-treatment index	.81	.35
Lesion-to-lesion index	.40	.17
Percent infections identified of contacts reported	45.0	29.9
Percent of contacts reported brought to treatment in primary or secondary stage	11.3	7.7
Number of contacts necessary to find *one* primary or secondary syphilis case	8.9	12.9

Six contacts brought to treatment with primary or secondary syphilis had no record of having been interviewed for contacts. However, of these six individuals, one had been treated by a private physician, four had been treated in Mississippi counties other than Quitman County, and one had gone outside the State. It is therefore felt that in this particular instance no negligence or oversight existed.

The following factors were identified as influencing the indices:

1. Of the contacts brought to treatment with open lesion syphilis, six did not name their informant as a contact. While this does not affect the lesion-to-lesion index or the accomplishment of contact investigation, it does suggest that some patients were careless or reticent about naming contacts or that the interview could have been more thorough.

2. Among the contacts of five patients, it was impossible to identify a case of early syphilis (with lesions or in the latent stage), even though all contacts named were examined. Since it would seem to be a truism that at least one case of early syphilis exists among the contacts of each primary or secondary case, we must accept these five investigations as failures.

3. For an additional 11 patients, for each of whom at least 1 contact was not examined, no case of early syphilis (lesion or latent) was found among the examined contacts. While it is realized that the infected contact may be among those not examined, these 11 cases must be considered failures in the contact investigation process.

Thus, among 89 patients with open lesion syphilis, it was impossible to identify a case of early syphilis in 16 patients (18 percent). If this fact had been known during the period of the project, presumably many of these patients would have been reinterviewed. It is believed that current appraisal of records and prompt reinterview of patients are requisites of effective contact investigation.

Summary

1. Three hundred and twenty contacts, reported by 89 patients with primary or secondary syphilis, were examined or their record identified (contact index, 3.595): 144 contacts were found infected with syphilis (epidemiologic index, 1.618); 72 new cases were brought to treatment (brought-to-treatment index, 0.809); 36 of the new cases were diagnosed in the primary or secondary stage of infection (lesion-to-lesion index, 0.404).

2. Distribution of contacts shows that more persons reported 2 contacts than any other number; however, 1 patient named 8 contacts, 1 named 9, and 1 named 11.

3. Comparison of results of contact investigation in Quitman County and in 26 other areas shows the following indices, respectively: Contact, 3.60 and 2.13; epidemiologic, 1.62 and 0.64; brought-to-treatment, 0.81 and 0.35; lesion-to-lesion, 0.40 and 0.17.

4. In Quitman County, 11.3 percent of contacts reported were brought to treatment in the primary or secondary stage of infection, as against 7.7 percent in the 26 other areas.

5. In spite of the accomplishments, it was felt that many potential open lesion cases of syphilis were missed.

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A Stable Control Serum for Standardizing the Sensitivity of Tests Used in the Diagnosis and Control of Syphilis[1]

George R. Cannefax, Bacteriologist, United States Public Health Service

The further standardization of laboratory tests used as aids in the diagnosis and control of syphilis is dependent upon the utilization of stable control serum of authoritatively established reactivity. A stable serum of known reactivity can and should be used daily to permit a check on the day-to-day sensitivities of all the serodiagnostic tests, colloidal reactions, and quantitative determinations of total protein. That these tests are not now controlled by the use of a stable serum of known reactivity and protein content is probably because of the general premise that reagin and other serum components have a degree of lability that will not permit long periods of storage without alteration of their properties.

Materials and Methods

The serum discussed in this article has apparently remained stable in its chemical and physical properties during storage at room temperature for a year. Room temperature was chosen since it would probably represent the severest test of temperature stability to which serum of this type would ever be subjected during shipment or prolonged storage. The only observed instability during storage has occurred in ampules in which the glass seals were broken.

Serum with a reagin titer of 512 Kahn units has been precipitated and the lipoids removed by the method of Hardy and Gardiner (*1*) in a cold (—20° C.) mixture of absolute ethanol and absolute diethyl ether after it had been previously concentrated to one-third its volume by placing the serum in cellophane tubing in front of a fan as originally described by Kober (*2*). The precipitated serum was filtered and washed with several washings of cold absolute diethyl ether, using a Buchner funnel and vacuum. The residual ether was removed by placing the funnel and precipitate in a vacuum desiccator over sulfuric acid. The dry, ether-free precipitate was reconstituted to the original volume of serum, and 5-ml. quantities were placed in ampules and shell-frozen, using ethanol and solid carbon dioxide, followed by dehydration with the cryochem apparatus. Prior to sealing the all-glass ampules, the residual moisture was removed by placing the ampules in a vacuum desiccator over phosphorus pentoxide for 48 hours.

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[1] From the U. S. Public Health Service Medical Center, Hot Springs National Park, Ark.: George R. Cannefax, Laboratory Director.

Acknowledgment.—This report would not have been possible except for the wholehearted support of, and participation by, all the persons who have been members of the laboratory staff during the past year and a half. The author is deeply grateful for the cooperation they have given this investigation and is indebted to the many clinicians and serologists who have given encouragement and helpful suggestions.

Table 1.—*Usual day-to-day results of tests. using the stable control serum*

Test procedure	Test results
Kolmer (spinal fluid test)	4 2 0 0 0 (tube readings).
Kolmer (serum test)	2 0 0 0 0 (tube readings).
Kahn standard	16+ to 21+.
Kahn quantitative	1:2 dilution, 2+ to 4+. 1:4 dilution, negative to 3+. 1:8 dilution, negative.
VDRL slide test (qualitative)	Positive.
VDRL slide test (quantitative)	1:2 dilution, positive. 1:4 dilution, negative or weak positive. 1:8 dilution, negative.
Colloidal mastic test	5554321000.
Spinal fluid total protein	60. mg. percent.

Table 2.—*Kolmer test results, using the stable control serum*

1947	Minutes[1]	Tube readings[2]	Minutes[3]	1948	Minutes[1]	Tube readings[2]	Minutes[3]
Mar. 17	30	2 0 0 0 0 4 2 0 0 0	15	Mar. 15	20	2 0 0 0 0 4 2 0 0 0	10
Mar. 18	20	2 0 0 0 0 4 2 0 0 0	10	Mar. 16	15	2 0 0 0 0 4 2 0 0 0	15
Mar. 19	20	2 0 0 0 0 4 2 0 0 0	10	Mar. 17	25	2 0 0 0 0 4 2 0 0 0	15
Mar. 20	20	2 0 0 0 0 4 2 0 0 0	10	Mar. 18	20	2 0 0 0 0 4 2 0 0 0	10
Mar. 21	15	2 0 0 0 0 4 2 0 0 0	10	Mar. 19	20	2 0 0 0 0 4 2 0 0 0	10

[1] The number of minutes of total secondary incubation required to yield the desired result.

[2] The upper figure indicates the result of the quantitative serum test; the lower figure the result of the quantitative spinal fluid test.

[3] The figures indicate the number of minutes of secondary incubation required for the antigen and other controls to hemolyze completely.

Results

One lot of processed serum has been used daily for the past year, to compare the day-to-day sensitivities of the Kahn diagnostic and quantitative tests, the Kolmer quantitative spinal fluid test, the qualitative and quantitative VDRL slide test, and colloidal mastic reactions, and as a control for the turbidimetric quantitative determination of spinal fluid protein. The tests have, in general, given results as shown in table 1 when the control serum has been diluted 1:100 with 0.85-percent sodium chloride solution.

Variations in the results shown in table 1 have occurred in most of the test readings throughout the year and a half that the serum has been used. It is not known whether the variations have been within allowable limits since limits of error have not been authoritatively established. The variations have been attributed to technical errors in certain tests, to errors perhaps inherent in the test procedure, and to a combination of these two sources of error. It is important to note that the use of the stable control serum has indicated that there were variations of which, in certain instances, we otherwise would have been unaware.

Kolmer Test Results Obtained With the Stable Serum

The Kolmer test results with the diluted stable serum, recorded in table 2, indicate that it is necessary to shorten or lengthen the secondary incubation time, depending upon the sensitivity of the hemolytic system, in order to stabilize the sensitivity of the test. The secondary incubation time may or may not be 10 additional minutes of incubation after the controls have hemolyzed, as now recommended for the Kolmer test. It will be noted, in table 2, that on March 17, 1947, the 10-minute requirement needed to be exceeded, and that on March 21, 1947, and March 16, 1948, less than the recommended secondary incubation time yielded the desired test sensitivity. Since either insufficient or excessive secondary incubation will affect the sensitivity of the test, it is apparent that an indicator of the proper secondary incubation time should be an integral part of the test procedure. Generally, the desired reading of the control serum has occurred 10 minutes after the controls have hemolyzed. However, the days that the adjustment of the hemolytic system has been either very sensitive or insensitive have conclusively demonstrated that an indicator of test sensitivity (stable reference control serum) is needed to produce a predetermined level of day-to-day sensitivity of the test.

Kahn Test Results Obtained with the Stable Serum

The control serum has been tested with approximately 2,000 mixes of Kahn standard antigen during the year that the serum has been used. Generally speaking, the test results, using the control serum, have been fairly constant with

Table 3.—*Kahn test results, using the stable control serum*

Date	Kahn standard				Kahn quantitative			
	A[1]	B[2]	C[3]	Report	1:2	1:4	1:8	Report
1947								
Mar. 17	±44	±44	16	Pos. 3	1	–	–	Neg.
	±44	±44	16	Pos. 3	±	–	–	Neg.
	±44	–44	16	Pos. 3				
Mar. 18	±44	–44	16	Pos. 3	1	±	–	Neg.
	–34	–34	14	Pos. 2	2	–	–	8 QKU.[4]
	–34	–34	14	Pos. 2				
	–34	–34	14	Pos. 2				
Mar. 19	±44	–44	16	Pos. 3	2	±	–	8 QKU.
	±44	±44	16	Pos. 3	4	2	–	16 QKU.
Mar. 20	144	144	18	Pos. 3	1	–	–	Neg.
	±44	±44	16	Pos. 3	1	±	–	Neg.
	±44	±44	16	Pos. 3				
Mar. 21	–14	–±4	9	Dbt. 1+	1	±	–	Neg.
	–34	–34	14	Pos. 2	±	–	–	Neg.
	–34	–34	14	Pos. 2	2	–	–	8 QKU.
1948								
Mar. 15	–44	–44	16	Pos. 3	2	1	–	8 QKU.
	–44	–44	16	Pos. 3	2	±	–	8 QKU.
	–44	–44	16	Pos. 3	2	–	–	8 QKU.
Mar. 16	–34	–24	13	Pos. 2	2	1	±	8 QKU.
	–44	–44	16	Pos. 3	2	–	–	8 QKU.
	–44	–44	16	Pos. 3				
Mar. 17	–34	–34	14	Pos. 2	2	–	–	8 QKU.
	–44	–44	16	Pos. 3				
	–24	–14	11	Pos. 2				
	–24	–14	11	Pos. 2				
Mar. 18	–24	–24	12	Pos. 2	2	1	–	8 QKU.
	–24	–14	11	Pos. 2	–	–	–	Neg.
	– –4	– –4	8	Dbt. 1+	–	–	–	Neg.
	– –4	– –4	8	Dbt. 1+				
Mar. 19	–34	–34	14	Pos. 2	2	±	–	8 QKU.
	–34	–34	14	Pos. 2				
	–34	–34	14	Pos. 2				
	–44	–44	16	Pos. 3				

[1] The figures represent the tube readings immediately after adding saline to the tubes.
[2] The tube readings 15 minutes later.
[3] Total number of pluses resulting from the combined readings. 1:2; 1:4; 1:8; dilution of the serum with saline. The figures represent the reading of each tube.
[4] Quantitative Kahn units.

both the diagnostic and quantitative Kahn tests. Occasionally, one or more antigen mixes during a given workday have resulted in a much less sensitive test. The findings recorded in table 3 are typical of the results observed and indicate that the serum possesses a satisfactory stability for use as a control serum for the Kahn test for at least 1 year.

VDRL Slide Test Results Obtained with the Stable Serum

The VDRL slide test has been very consistent in sensitivity when the stable serum has been used quantitatively as a standard control. During the period that the control serum has been tested with the VDRL slide test, 236 antigen suspensions have been prepared. Each antigen emulsion has been tested with the control serum before performing the routine tests. In no instance has an antigen emulsion been discarded because of improper sensitivity. The results obtained with the stable serum and the VDRL slide test are shown in table 4.

It will be noted that the dilutions shown in table 4 are spaced more closely than the usual dilutions of the 1 : 2, 1 : 4, 1 : 8, etc. The test results a year apart would have been identical, in terms of positive, weak positive, and negative, if the serum had been tested undiluted, 1 : 2, 1 : 4, and 1 : 8.

The findings recorded in table 4 are representative and indicate that the serum maintained a satisfactory stability for use as a control serum for the VDRL slide test for at least 1 year.

Colloidal Mastic Test Results Obtained With the Stable Serum

The colloidal mastic test has shown considerable variation in sensitivity when the stable serum has been used in proper dilution as a control. Generally, the reaction with the control serum has been 5554321000. The changes in sensitivity observed with the test have been, in most instances, toward greater sensitivity, e. g., 5555543210. When very sensitive runs of tests have been observed, all spinal fluids showing mastic changes have been retested. In some instances, the hypersensitivity of the tests would have been noted without the use of the control. However, the control serum has shown increased sensitivity of the test when the over-all run of tests did not indicate test oversensitivity.

A comparison, as shown in table 5, of the colloidal mastic test results in March 1947 and March 1948 indicates that the serum maintained a satisfactory stability during this period, since the results are similar.

Table 4.—*VDRL slide test results, using the stable control serum*

Date	Dilution							
	Undiluted	1:2	1:3	1:4	1:5	1:6	1:7	1:8
1947								
Mar. 17	[1] P	P	[2] WP	WP	[3] RN	[4] N	N	N
Mar. 18	P	P	P	WP	RN	N	N	N
Mar. 19	P	P	P	WP	RN	N	N	N
Mar. 20	P	P	P	WP	RN	N	N	N
Mar. 21	P	P	WP	WP	RN	N	N	N
1948								
Mar. 15	P	P	P	WP	RN	N	N	N
Mar. 16	P	P	P	WP	RN	N	N	N
Mar. 17	P	P	P	WP	RN	N	N	N
Mar. 18	P	P	WP	WP	RN	N	N	N
Mar. 19	P	P	P	WP	RN	N	N	N

[1] P: positive.

[2] WP: weak positive.

[3] RN: rough negative. (RN is never reported as such. Reactions of this type are reported negative unless they are shown to be of the zone type which is frequently found with highly positive serum.)

[4] N: negative.

Table 5.—Colloidal mastic test results, using the stable control serum

Date	Mastic test	Date	Mastic test
1947		*1948*	
Mar. 17	5555310000	Mar. 15	5555432100
Mar. 18	5554310000	Mar. 16	5554321000
Mar. 19	5554321000	Mar. 17	5555421000
Mar. 20	5555421000	Mar. 18	5554321000
Mar. 21	5555532100	Mar. 19	5555432100

Table 6.—*Total protein determinations, using the stable control serum*

Date	Milligrams percent protein	Date	Milligrams percent protein
1947		*1948*	
Mar. 17	62.0	Mar. 15	60.2
Mar. 18	59.5	Mar. 16	61.1
Mar. 19	57.0	Mar. 17	62.7
Mar. 20	60.0	Mar. 18	58.2
Mar. 21	57.0	Mar. 19	63.0

Spinal Fluid Total Protein Determination Obtained with the Control Serum

Spinal fluid total protein determinations have been controlled by use of the stable serum. Micro-Kjeldahl analysis gave a total protein result of 6.0 percent when the dried serum was reconstituted to original volume. A 1 : 100 dilution containing 60.0 mg. percent protein has been used daily as a control. A tabulation of the daily results, a year apart, is shown in table 6. These results indicate that the serum within the specified limit has maintained sufficient stability to serve as a standard control for this test.

Discussion

The positive control serum that serologists have so long considered a necessary part of the serodiagnostic tests is not an adequate control. It usually contains many times the amount of reagin needed to give a weakly positive test result for the qualitative detection of reagin, and it does not serve as an indicator of the level of sensitivity of the quantitative tests. The adoption of a stable serum of known reactivity for use as a control would be a forward step in stabilizing the sensitivity of the various tests.

Stable control serum can be relied upon to indicate that a test has been performed within reasonable limits of variation. The allowable limits of error must be authoritatively established with the quantitative tests. It does not appear possible to attain this necessary requisite for the proper performance of quantitative tests by any other means than the use of a stable control serum. The limits of variation that could be accepted as satisfactory may of necessity be established for each test procedure. It would appear that the author serologists are the logical authorities for establishing the acceptable limits of error or variation of their respective tests. The colloidal reactions and spinal fluid total protein determinations might require the establishment of limits of error by a cooperative investigation by several laboratories, each using the same lot of stable serum for their tests.

If the author serologists would certify control serum (as they presently certify antigens) to be of standard reactivity, a check could then be established on the proper use of the standard antigen. Obviously, a standard antigen that is misused by the improper conduct of a test procedure cannot result in standard test performance. The only way to know if a standard antigen is properly used is by the use of a control serum of known reactivity. No doubt, the author serologists in a further effort to improve the performance of their tests will be as eager to certify stable control serum as they have been to approve antigens prepared by biologic supply firms.

The stable control serum has served as a source of known protein concentration for calibrating a photoelectric comparator for the quantitative determination of protein in spinal fluid. Used daily, the serum has served as a check on the technical conduct of the test and on the electronic functioning of the photoelectric comparator.

The stable control serum, in proper dilution, has served a useful purpose in being a constant reference control for adjusting new lots of gum mastic solution to the same sensitivity of previous lots. The control, used daily, has not prevented the occasional occurrence of oversensitive mastic tests, but it has made possible the immediate detection of variations in test sensitivity.

Conclusions

A method of preservation of serum for use as a control for the flocculation tests, complement-fixation tests, colloidal reactions, and spinal fluid total protein determinations has been presented.

The necessity for the adoption of a standard control serum for controlling the sensitivity of qualitative and quantitative tests has been discussed.

Evidence has been presented that the serum has maintained satisfactory stability for a minimum of 1 year.

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CURRENT NOTES AND REPORTS

The New Columbia University Communication Materials Center

Encouraged by the popularity and effectiveness of a series of radio transcriptions designed for VD case finding in 1948, the Columbia University Press, with assistance from the State of New Jersey and the United States Public Health Service, has set up the Columbia University Communication Materials Center. The objective of the Center is to provide, on a nonprofit basis, public appeal materials for the use of State and local health departments and other public service agencies. Initially, the Center is concentrating on the production of such materials for VD case-finding drives.

The Center will maintain only a small staff. Its policy is to contract for the best talent available for any particular assignment, thus eliminating the overhead involved in maintaining a large staff. In addition to availing itself of the effective distribution system of the Columbia University Press, the Center will also draw on the services of the University's School of Journalism, School of Public Health, Radio Bureau, and Visual Aids Center.

The Center arranges for the production and distribution of popular materials for all types of communication channels—

radio, movies, television, newspapers, display advertising, juke boxes, and printed promotional materials. The following items are available for syphilis case finding drives this summer:

1. *Radio.*—Six transcribed 15-minute radio dramatizations and 20 spot announcements of 30 seconds each, accompanied by an assortment of promotional materials, including press releases and mats for local newspaper advertisements regarding these radio programs.

2. *Movies.*—A series of 5-minute movies for use in commercial theaters, over television, and before special groups alerting the public to the dangers of untreated syphilis and urging those who suspect infection to seek diagnosis and treatment. These movies feature well-known entertainers or personalities prominent in the world of sports. Each star appears in a short scene featuring him in the role for which he is popularly known, after which he makes a brief statement about the VD problem.

3. *Printed materials.*—Posters, car cards, decal stickers for washrooms, one basic pamphlet on syphilis (for use primarily by health departments and radio stations in answering requests for general information), a series of pamphlets designed for special groups, such as industrial workers, women, young people, and tavern, restaurant, and diner patrons. Each piece of printed material reiterates in color, format, and theme the message of the basic pamphlet and the appeal of the case-finding campaign.

4. *Reprint service.*—Reproduction and wider distribution, when permissible, of materials which have been particularly successful in certain localities. Among these are the films, "Feeling All Right," which was produced for the State of Mississippi by the Southern Educational Film Production Service of the University of Georgia, and "The Big Fight," starring Joe Louis, produced by the New York City Health Department.

A catalogue, a price list, and sample kits of these materials have already been distributed to State and local health departments throughout the country, and orders are being filled currently.

To States and communities particularly, the Center constitutes a real service. Because of the highly competent consultation service available to it, its facilities for the use of top-flight talent, and the benefit of large-scale production, the Center is equipped to furnish highly effective materials quickly and cheaply.

Heading the Center as Supervisor of Special Projects is Erik Barnouw, well-known radio writer, producer, and Director of the Columbia University School of Radio. Mr. Barnouw's background includes experience in advertising and publication. He is currently national president of the Radio Writer's Guild.

Manager of Special Projects is Betty Ballantine Hogan, graduate of the Columbia University School of Journalism and former feature writer with the San Francisco News. She has been associated during the past 10 years with public relations and advertising firms on the West Coast and in New York City.

Herbert R. Jensen is Manager of Columbia University Educational Films, Communication Materials Center. Mr. Jensen was formerly Director of Research of National Educational Films and also formerly Survey Director of the National Research Council Committee on Scientific Aids to Learning.

"Casanova—The Tale of a Mouse"

The latest VD educational effort of the Navy is a comic booklet entitled "Casanova—The Tale of a Mouse," prepared by a former naval officer, Mr. Will Anderson, in consultation with naval authorities. This booklet, designed for both civilian and military distribution, is a fictional story in verse form, subtly illustrated.

VD Radio Programs "Tops"

VD radio programs rated high with the judges of the 13th Annual American Exhibition of Educational Radio Programs at Ohio State University recently. Of the 57 firsts, ABC's 1-hour documentary, "VD—The Conspiracy of Silence," shared top honors with NBC's "Living—1949" in the category of public affairs, drama. The Columbia University VD case-finding series received one of the nine special awards.

Recipients of awards were culled from an evaluation of 761 programs aired in the United States and Canada. Of these, 201 were national network shows, and 560 were regional, local, and transcribed shows.

Summary of the Report of the Second Session of the Expert Committee on Venereal Diseases, World Health Organization

The Expert Committee on Venereal Diseases met October 15–19, 1948, at L'Office Internationale d'Hygiene Publique, Paris. Dr. J. F. Mahoney served as chairman and Dr. T. Guthe as secretary. Dr. G. L. McEligott served as chairman during the discussion of the Brussels Agreement and during the seventh meeting of the session. A summary of the discussion and recommendations follows.

With the advent of penicillin therapy the methods previously employed in the control of early syphilis appear to be undergoing changes. It is possible that the following far-reaching implications may be attached to the widespread use of antibiotic therapy in early syphilis:

1. A reduction in the incidence of the disease due to the ability of antibiotic therapy to curtail rapidly the infectious stages of the disease.

2. A reduction in the number of severe complications and a minimizing of the destructive capacity of late syphilis.

3. A major alteration in the demands which will be made upon the serologic laboratory of the future in regard to the diagnosis of the disease and the guidance of therapy.

One of the first objectives of WHO in its program should be the initiation of control work in regions where syphilis is highly prevalent and where only limited venereal disease services exist. The Committee considers that foreshortened ambulatory treatment of early syphilis with penicillin offers possibilities for large-scale treatment in terms of population groups.

The establishment of widespread control facilities is made difficult by the limited availability of penicillin, shortage of experienced personnel, and failure of current medical literature to reach the profession during recent years.

The Committee recommends that WHO collect further information on penicillin production and distribution; that steps be taken to insure a wider availability of the drug; that rehabilitation of the United Nations Relief and Rehabilitation Administration plants be considered as soon as the contemplated survey of these plants has been carried out, and that this matter be studied also by the United Nations Economic Commission for Europe; and that WHO be prepared to advise on the quality and standards of penicillin products.

Applications for fellowships should be more rigidly examined, especially as regards the adaptability and proficiency of the candidate in the specialty selected. Further criteria should be established on the basis of medical, scientific, and other accomplishments, linguistic ability, etc. Reports should be submitted on benefits derived from the studies of the fellow during and at the end of the training period. Fellows should study at centers recommended by WHO. The needs of governments should be met as far as possible, particular attention being directed to the granting of such fellowships as are necessary to implement venereal disease programs carried out with the assistance of WHO or recommended by the Joint Committee on Health Policy of WHO and United Nations International Childrens' Emergency Fund (UNICEF).

The Committee recommends that a possibly increased demand for expert consultants be met as far as possible in 1949 and 1950; and that services be provided for lecturing at postgraduate venereal disease control centers and for consultation on diagnostic, therapeutic, legal, social, or administrative aspects of venereal disease control.

The basis for a mass attack on syphilis can be laid by well-supplied and well-equipped demonstration and consultation teams. The Committee recommends that in 1949 one team be allocated to India and a second to Egypt. Supplies and equipment should be made available to the teams on a broader scale than proposed under the 1949 program, while increased team activities should be planned for 1950 and later.

The Committee recommends that WHO study ways and means for an increased dissemination of technical information on venereal disease control methods. It further recommends that a temporary study group, consisting of a limited number of outstanding venereologists, be established in 1949 to evaluate the venereal disease control methods in the United States as to their effectiveness in national and international programs.

Planning in the field of serology has been complicated by the demands made by penicillin therapy, and some revision in the WHO serologic program as originally proposed may be required. There seems to be reasonable evidence that cardiolipin-lecithin antigen, because of greater specificity, will replace the older types of antigen. The promotion of the use of cardiolipin-lecithin antigen throughout the world may well become a worthwhile activity of WHO.

Many discrepancies in the serology of syphilis result from the lack of uniformity in the level of reactivity of the several test methods. It is essential to determine the level of reactivity which contributes most in terms of clinical syphilis and which, at the same time, escapes the influence of those nonsyphilitic diseases and environmental factors believed responsible for false positive serologic reactions. The Committee recommends the establishment of the subcommittee on serologic and laboratory aspects of syphilis, proposed in the adopted program of the Expert Committee of the Interim Commission, and the formulation as soon as possible of a preliminary program for the conduct of an International Serological Laboratory Conference for consideration by the Expert Committee on Venereal Infections.

Thus far, the concern expressed in many quarters that penicillin-resistant gonorrhea and penicillin-resistant syphilis might develop has not been substantiated. Ninety-five percent, or more, of patients treated for gonorrhea with adequate schedules of amorphous or crystalline penicillin will be cured. While there are varying opinions as to the actual status of penicillin in the treatment of syphilis, general agreement appears to exist on the advantages of the drug in the therapy of prenatal and congenital syphilis and in the rapid curtailment of the infectious stages of early syphilis. Although consolidation through additional therapy with arsenicals and/or bismuth is considered desirable by several groups of investigators (particularly in Europe), the incorporation of oxophenarsine hydrochloride and bismuth in penicillin therapy has not reduced significantly the failure rates, but has transformed a practically innocuous treatment method into a more dangerous one.[1]

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[1] Examples of acceptable penicillin treatment schedules for syphilis and gonorrhea, together with those used in the Polish antisyphilis campaign, will be found in Annex No. 2, page 179.

In the opinion of the Committee, WHO should encourage voluntary health organizations to assume responsibility for informing and gaining the support of the public in venereal disease control programs. The Committee suggests that the material gathered by the Danish Union Against Venereal Disease, in its attempt to measure the effects of a venereal disease campaign, be made available to other health administrations.

The Committee reaffirms its belief that countries should be encouraged to record at least basic data on the incidence of venereal diseases, with emphasis on that of syphilis. The Committee suggests that WHO clarify the provision of "Free and confidential treatment of venereal diseases" found in the draft-text discussed by the Social and Economic Council at its seventh session in Geneva.

The Committee believes that assistance in combating prenatal and congenital syphilis should preferably be granted to countries where a structure for venereal disease control exists and where the introduction of penicillin treatment would serve to stimulate the control work in such a way that a mass attack against syphilis might be carried out; or where there are problems of endemic syphilis; or where it is desirable to encourage the development by governments of broader venereal disease control programs.

The Committee recommends that WHO be prepared to provide such qualified personnel as will be required to conduct surveys and to initiate and follow up prenatal and congenital antisyphilis programs recommended by the Joint Committee on Health Policy of UNICEF and WHO and accepted by the executive boards of these two organizations.

The Committee is in favor of the participation of WHO in the Tenth International Congress on Dermatology and Syphilology scheduled to meet in 1950.

Principles adopted by the Interim Commission and by the Health Assembly (outlined in the report of the Expert Committee of the Interim Commission) were taken as a basis by the Committee for the drafting of International Regulations for Venereal Diseases, including matters contained in the Brussels Agreement. The Committee recommends that a provisional text for International Regulations on Venereal Diseases be prepared for circulation to members of WHO and that a final draft be submitted to the Health Assembly.

Information available indicates a decrease in incidence of venereal disease in rural and inland areas, but no similar decrease in the ports. This emphasizes the problem of maritime transfer of venereal disease from one country to another. Hence the Committee recommends that a special investigation be established in a major port in northern or southern Europe or in the Far East, as a collateral to the implementation of a revised Brussels Agreement. Some international aspects of the maritime venereal disease problem are of a regional character. Therefore the Committee further recommends that the relevant authorities in Belgium, France, Germany, Holland, and Switzerland be approached by WHO with a view to the establishment of a commission composed of representatives of those countries, to study and recommend measures for coordination of venereal disease control in the Rhine area.

Bejel and related spirochetoses are a problem of considerable importance to the health of the people in tropical and subtropical areas, and their manifestations in different environments have been studied only to a limited extent. The Committee recommends that the problem of bejel (the nature and extent of this and related spirochetoses) be studied by WHO and that it be made a separate activity of WHO in view of the predominantly nonvenereal nature of these conditions.

The Committee expresses its commendation on the progress made since the Polish antisyphilis plan was put into operation at the beginning of the year. The treatment of 43,000 cases of syphilis and 27,000 cases of gonorrhea up to August represents a public health achievement. The program could not have been carried out except through a systematic large-scale approach, through case finding, and foreshortened treatment methods

In view of the technical aspects and scope of the problems of venereal disease control in relation to the international program of WHO, a representative advisory expert body of specialists in the various departments of control work is required. The Committee recommends that the WHO Expert Committee on Venereal Infections be composed of 10 members and that a subcommittee on serologic and laboratory aspects be established, consisting of no more than 4 members.

A summary of several of the annexes is presented below.

Annex No. 1

Under the WHO venereal disease program 32 governments requested services, a summary of which follows: expert advice (6); fellowships (21); demonstration teams and experts (18); equipment and supplies (4); and technical information (21).

Annex No. 2

Examples of acceptable treatment schedules with penicillin

Disease	Drug	Dosage per injection	Total injections	Total dosage
Gonorrhea	Penicillin (aqueous)	50,000 units at 0 hour 50,000 units at 1 hour 100,000 units at 2 hours	3	200,000 units.
	Penicillin in oil and beeswax.	300,000 units	1	300,000 units.
Early and prenatal syphilis (also other forms, except central nervous system, cardiovascular, and congenital syphilis).	Penicillin G (aqueous).	50,000 units q.2 hours for 90 injections.	90	4.5 million units.
	Penicillin G in oil and beeswax (P. O. B. liquid).	500,000 units q.24 hours for 10 injections.	10	5 million units.
	Procaine penicillin G in 2 percent aluminum monostearate.	600,000 units q.24 hours for 3 injections.	3	1.8 million units.
		600,000 units twice weekly for 2 weeks.	4	2.4 million units.
Congenital syphilis (early)	Penicillin G (aqueous).	85,000–100,000 units per pound of body weight, divided into from 85 to 100 doses; each dose q. 2 hours.		

Treatment schedules used in the Polish antisyphilis program

Stage of disease	Drug	Dosage per injection	Total injections	Total dosage
Seronegative primary	Penicillin in oil and beeswax.	300,000 units q. d.	10	3,000,000 units.
	Bismuth	0.2 gm. on 1st, 4th, 7th, and 10th days.	4	0.8 gm.
Seropositive primary; secondary; early latent.	Penicillin in oil and beeswax.	300,000 units q. d.	14	4,200,000 units.
	Mapharsen	0.06 gm. on 4th, 7th, 10th, 13th, 16th, 19th, 22nd, 25th, 28th, and 31st days.	10	0.6 gm.
	Bismuth	0.2 gm. on 4th, 7th, 10th, 13th, 16th, 19th, 22nd, 25th, 28th, and 31st days.	10	2.0 gm.
Prenatal	Penicillin in oil and beeswax.			6,000,000 units.
Congenital	Penicillin in oil and beeswax.	20,000 units per kg. of body weight q. d.	10	200,000 units per kg. of body weight.

Annex No. 3

Follow-up results of penicillin therapy in early syphilis [1]

[Total dosage, 7,200,000 units (200,000 units every 2 hours for 36 doses)]

Period	Number treated	Number observed	Number positive	Number negative	Number re-treated
Months					
1–4	451	373	240	127	6
5–8	451	304	97	201	6
9–12	381	182	36	142	4
13–18	242	82	11	71	0

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[1] Venereal Disease Research Laboratory, U. S. Public Health Service, U. S. Marine Hospital, Staten Island 4, N. Y.

Annex No. 6

Progress Report on the Polish Antisyphilis Campaign

In January 1948, plans for the Polish antivenereal campaign were presented to the Interim Commission's Expert Committee, providing for the following: (1) Planning and elaboration of program; (2) organization of treatment facilities; and (3) implementation of program through case finding, treatment, health education of the public, and other means. The first phase was completed in January. By April, 80 percent of the second phase was completed, 300 county health centers having been established. In the organization of these health centers, 240 physicians, 300 nurses, and 250 public health nurses or social workers were recruited. Free courses were opened to all physicians. By July 1948, 480 physicians had attended the 16 courses covering diagnosis, treatment, and social aspects of venereal disease control. Similar courses were organized for nurses and social workers

A scarcity of essential diagnostic and other equipment was encountered. By October, 42 darkfield microscopes had been provided. Limited availability of laboratory equipment restricted the quantitative serologic follow-up of penicillin-treated patients.

Mobile units were sent into areas where a high venereal disease rate was suspected; the entire population of the area was examined and cases of syphilis were referred to the nearest health center. These units also distributed antivenereal literature and films, and their medical officers lectured the public.

Some health centers started operation in January and February 1948, but action on a large scale was not begun before April, when considerable supplies of penicillin were received.

The educational campaign was also started in April through the newspapers, the radio, and the distribution of booklets and posters. The educational campaign was so effective that by the end of June there was insufficient penicillin to treat all patients reporting. To the original 10-day penicillin therapy were added 10 injections of mapharsen (0.06 gm.) and 10 injections of bismuth (0.2 gm.), administered over a period of 30 days. This compromise in therapy was necessitated by the opinion of many practitioners that penicillin had not yet proved its value for exclusive use in syphilotherapy.

The Chediak method was found to be the most practicable mass-screening serologic test for syphilis. Positive reactions were further checked with the Kahn flocculation and the Wassermann complement-fixation procedures. Another case-finding mechanism to be employed was the tracing of infectious contacts (10,000 of the 18,000 reported were found to be positive).

The Polish Ministry of Health is of the opinion that the following points should be stressed: intensification of public education; provision of equipment for health centers and laboratories; strengthening of case-finding and follow-up mechanisms, particularly with reference to the tracing of infectious contacts; extensive postgraduate training on the various aspects of venereal disease control; extension of the network of treatment facilities; and careful study of the value of serologic tests in mass screening of syphilis.

CURRENT LITERATURE

NOTE: Abstracts of any article listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

ACTA DERMAT.-VENEREOL., OSLO

Arthro-syphilis congenita tardiva et acquisita et arthro-metasyphilis. Halfdan Sundt. 28: 1–419, 1948. (Supplement 20.)

ACTA DERMAT.-VENEREOL., STOCKHOLM

The effect of penicillin on late congenital syphilis, with special reference to the Wassermann reaction. Einar Hollström and Stig Hard. 28: 560–570, Fasc. 6, 1948.

Comparative investigations on gonorrhea treated with penicillin with single doses and multiple doses. Torsten Romanus. 28: 597–600, Fasc. 6, 1948.

AM. J. DIS. CHILD., CHICAGO

Complications of vaccination against smallpox. [Syphilis.] Morris Greenberg. 76: 492–502, Nov. 1948.

AM. J. M. SC., PHILADELPHIA

Effects of myanesin upon the central nervous system. [Tabes.] G. D. Gammon and J. A. Churchill. 217: 143–148, Feb. 1949.

*Penicillin syphilotherapy administered during pregnancy. A study of 149 pregnancies during which penicillin was given for early maternal syphilis. Harold A. Tucker. 217: 157–161, Feb. 1949.

Penicillin syphilotherapy administered during pregnancy. A study of 149 pregnancies during which penicillin was given for early maternal syphilis. Harold A. Tucker. Am. J. M. Sc., 217: 157–161, 1949.

The author presents a report of results obtained between October 1943 and March 1948 in 149 women treated with penicillin for concomitant early syphilis and pregnancy in the Johns Hopkins Hospital. Twenty-three of these were white and 126 were Negro.

In several, especially early in the study when comparatively small amounts of penicillin were administered (i. e., less than 3,000,000 units), mapharsen and bismuth were given concurrently. Various dosage schedules were used, ranging from 0.6 to over 5.0 million Oxford units of penicillin. In all cases the antibiotic was given in aqueous solution, intramuscularly every 2 or 3 hours for 7.5 to 15 days. Six women required re-treatment for relapse or reinfection, seroresistance, or serorelapse. In all other patients, the intensive routine of prenatal examinations did not disclose indications for re-treatment. In this study, 73.4 percent of the patients were treated during or after the fifth month of gestation.

Two abortions occurred. In neither was there evidence of syphilis, and both mothers had completed syphilotherapy prior to these disasters. There was one neonatal death, due to sickle-cell anemia, in a full-term Negro infant. Sixteen infants were premature, but all survived. Neither maternal disease nor penicillin therapy could be incriminated as the cause of prematurity. The author states that the incidence of prematurity probably did not differ significantly from the expected incidence in a similar, but nonsyphilitic, group of mothers.

On the basis of clinical, serologic, and/or roentgenologic evidence through the first 4 months of life or longer, treatment for congenital syphilis was not indicated in any of the surviving infants.

The author compares results obtained in this series with those reported in the literature and concludes that data obtained in this study strongly support the belief that penicillin (combined with intensive posttreatment serologic and clinical study), is the current treatment of choice for the syphilitic pregnant woman.

No patient in this series who was given 4,000,000 units or more required re-treatment. The author feels, therefore, that a total amount of 4.8 million units or more, without supplementary metal chemotherapy, is entirely adequate for the treatment of early (or late) syphilis in the mother, the prevention of transmission of syphilis to the uninfected fetus, and the cure of congenital syphilis in the fetus if infection has already taken place.

AM. J. M. TECHNOL., LAFAYETTE

Hemagglutination. General Principles. [Syphilis.] I. Davidsohn. 15 : 13–18, Jan. 1949.

AM. PRACT., PHILADELPHIA

Advances in treatment of neurologic diseases. [Syphilis.] Alexander Silverstein. 3 : 344–349, Feb. 1949.

BULL. GEORGETOWN UNIV. M. CENTER, WASHINGTON

Some practical considerations in the diagnosis and treatment of syphilis. Pasquale J. Pesare and Mario Mollari. 2 : 84–89, Oct.–Nov. 1948.

The clinical anatomy of the visual system. [Syphilis.] Othmar Solnitzky. 2 : 90–109, Oct.–Nov. 1948.

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GAZ. MED. PORTUGAL, LISBON

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HAWAII M. J., HONOLULU

Five years of heart disease in Hawaii. [Syphilis.] Morton E. Berk and Alfred S. Hartwell. 8 : 177–180, Jan.–Feb. 1949.

HEALTH NEWS, ALBANY

Prevention of treatment failure in syphilis. James H. Lade. 26 : 10–14, Feb. 1949.

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Public health and the prevention of blindness. [Ophthalmia neonatorum.] 20 : 96, Dec. 15, 1948.

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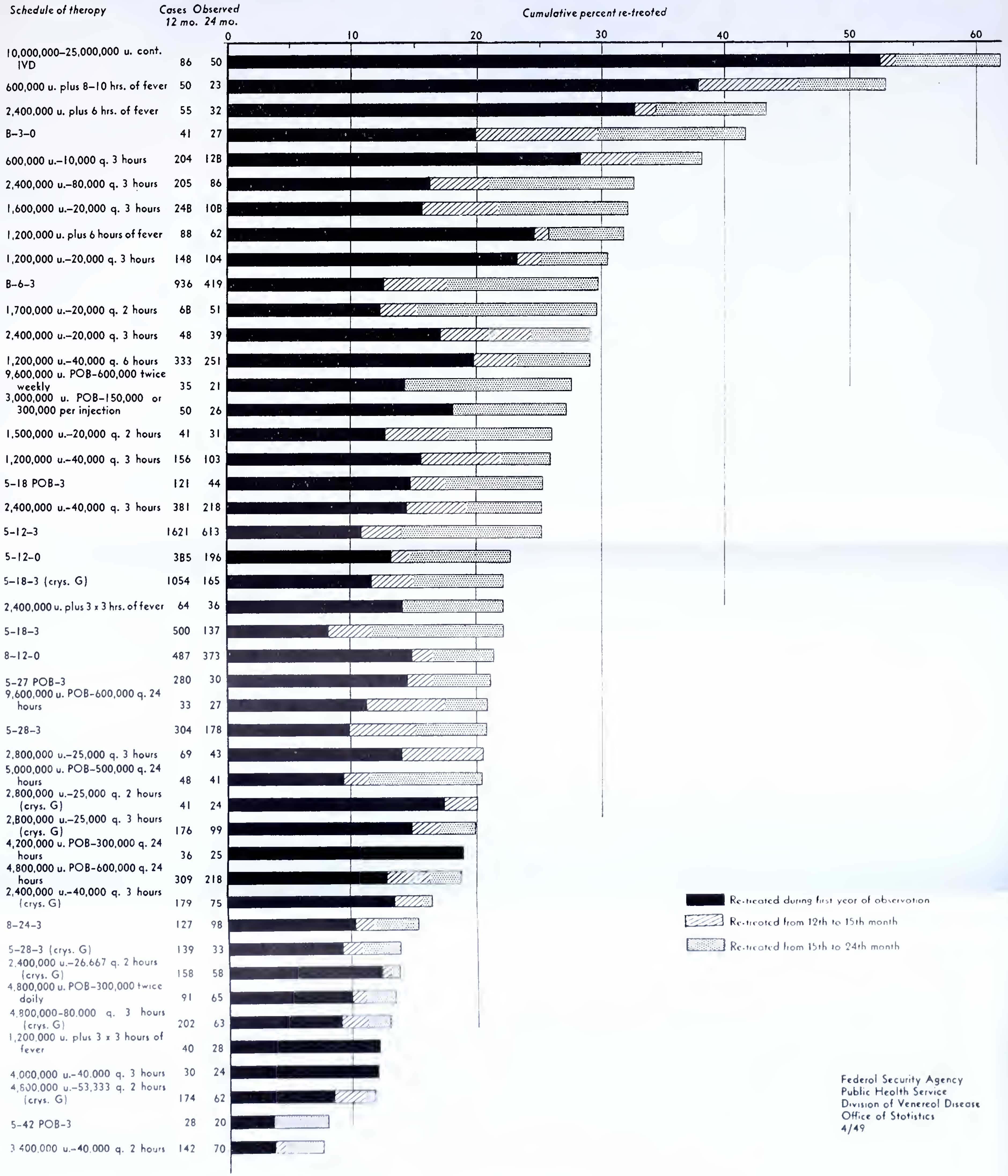
The possible viral nature of certain manifestations appearing simultaneously on genitalia, eyes, joints and other structures. [Lymphogranuloma venereum.] Waldemar E. Coutts. 14 : 173–186, Oct.–Dec. 1948.

COMPARATIVE EFFICACY OF VARIOUS PENICILLIN SCHEDULES IN THE TREATMENT OF SECONDARY SYPHILIS



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The JOURNAL *of* VENEREAL DISEASE INFORMATION

Volume 30 July 1949 Number 7

EDITORIAL

Is the Incidence of Syphilis Decreasing? 185

ORIGINAL ARTICLES

Reports of the North Carolina Syphilis Studies. II. An Evaluation of Case-Finding Measures in Multiple Episodes of Infectious Syphilis 187
John J. Wright, M. D., M. P. H.
Cecil G. Sheps, M. D., M. P. H.

Serologic Activity of Dipalmityl Lecithin. Preliminary Report . . . 194
Arthur A. Rosenberg, *Serologist*

Mass Public Venereal Disease Education—Ohio Fairs 196
Charles R. Freeble, Jr., M. D.
Earl O. Wright, *Health Program Representative*
Robert S. Bogue

CURRENT NOTES AND REPORTS 199

CURRENT LITERATURE 201

STATISTICS

Cases of Acquired Syphilis Reported by States and Territories, Fiscal Year Quarters 1941 to Date 209

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Editorial

Is the Incidence of Syphilis Decreasing?

The reported civilian case rate of primary and secondary syphilis in the United States is the lowest since reporting by stage began in 1941, and is only approximately 50 percent of what it was at its peak in the first quarter of the fiscal year 1947. This is shown graphically by the chart on page 209. Similarly the Army and Navy have shown decreases in the syphilis discovery rate over the same period. Does this mean that the incidence of syphilis is reduced in the United States? Many factors must be considered before an answer can be attempted.

1. The reported rate of primary and secondary syphilis measures the rate of discovery, not the incidence rate. As long as the discovery rate of early latent syphilis exceeds the discovery rate of open lesion syphilis we must assume that more than half of the cases of syphilis go into the latent stage undiscovered. The recent discovery rate of early latent syphilis has shown slight decreases, which would lend support to the thesis of diminished incidence.

2. A let-up in case finding would result in decreased diagnosis of primary and secondary syphilis even if no decrease occurred in the incidence of the disease. Since the fiscal year 1947, there has been no decrease in case-finding activity as measured by the number of diagnostic observations for venereal disease reported by public clinics in the United States as a whole. Moreover, contact investigation has improved and the medium of public appeal emphasized. It is the opinion of workers in the field that case-finding efforts are continuing on at least as high a level as hitherto.

3. The widespread use of penicillin in the therapy of gonorrhea may mask simultaneously acquired syphilis. It is estimated that the incidence of syphilis simultaneously acquired with gonorrhea does not exceed 3 percent. Moreover, treatment of gonorrhea is more likely to abort syphilis than to mask the early symptoms. Follow-up of persons with penicillin-treated gonorrhea who were separated from the Armed Forces did not reveal a significant amount of penicillin-masked syphilis.

4. The widespread use of penicillin for reasons other than venereal disease may be causing a change in the characteristics of early syphilis with less pronounced or nonexistent lesions. The decrease in latent syphilis discovered would seem to indicate that this explanation, as well as that in the preceding paragraph, cannot account for all the decrease in primary and secondary syphilis discovered.

5. Due to the development of shorter schedules of therapy, the treatment of syphilis may be shifting from public facilities to private physicians, who presumably do not report as completely. As a matter of fact, the number of cases of primary and secondary syphilis reported by private

physicians has decreased to the same extent as that reported by the clinics. So presumably the explanation does not lie in any shift from public treatment facilities.

We are, therefore, faced with evidence of decreased incidence of syphilis in those communities in the Nation that have case-finding programs and reporting systems. Does this mean that the incidence of syphilis has also decreased in those areas of the country that do not have venereal disease case-finding programs, the so-called "unorganized counties"? In the May issue of THE JOURNAL OF VENEREAL DISEASE INFORMATION, a case-finding project in an unorganized county in Mississippi during the period September 1947 through June 1948 was described. Case finding of primary and secondary syphilis increased more than 100 percent in this county over the previous year, whereas in a similar county, without a special program, the reported primary and secondary cases dropped 50 percent or approximately the same as in the Nation as a whole.

There are, therefore, areas in the United States which are not exposed to case-finding methods and in which syphilis goes undiscovered and untreated. We cannot be complacent and talk about reduction of incidence of syphilis in some areas of the United States as long as the disease is going unchecked in others.

One of the major problems facing venereal disease control officers today is still the problem of "the undiscovered."

THEODORE J. BAUER, *Medical Director*
Chief, Division of Venereal Disease

Reports of the North Carolina Syphilis Studies[1]

II. An Evaluation of Case-Finding Measures in Multiple Episodes of Infectious Syphilis[2]

John J. Wright, M. D., M. P. H., and Cecil G. Sheps, M. D., M. P. H.

Introduction

In a previous article (*1*), the authors discussed the importance of careful evaluation of the effectiveness of various case-finding measures in newly discovered cases of syphilis. This report is of a similar analysis of 142 cases of infectious syphilis, due either to relapse or to reinfection, with lesions visible to the patient, which occurred in patients who had received previous treatment for syphilis. Inasmuch as all the patients involved in this series had been given previous treatment, they all had received a measure of directed venereal disease education. It might, therefore, be expected that such individuals would present a different type of problem so far as the relative effectiveness of various case-finding procedures was concerned.

Method of Study

The North Carolina Syphilis Studies and their field of operation have been described in a previous article (*1*). The data presented here include all Negro cases registered with the Venereal Disease Clinic of the Durham City and County Health Department during 1944 through 1947. The patients selected met the following criteria:

1. Each had a history of at least one previous diagnosis of syphilis and treatment.

2. Each had a current diagnosis of primary or secondary syphilis, either reinfection or infectious relapse.

3. Each had one or more lesions visible to the patient at the time of diagnosis.

Cases of serorelapse without lesions and cases in which the lesions were not visible to the patient, such as intravaginal lesions, were not included. For the purposes of this study, no attempt was made to differentiate between relapse and reinfection. The data used were secured from the clinical record and from the special epidemiologic record form designed for research purposes and completed at the time of interview. It is believed that each case was assigned to the correct "reason for admission," because special attention was paid to this matter as part of the research being conducted by this group. This analysis was restricted to Negro cases because there were insufficient cases among white persons to justify studying the latter.

Classification of Case-Finding Methods

The classification of case-finding methods is a functional one in terms of what brought the patient to recognition, regardless of the referral agency; it falls into three groups, each requiring quite different activities on the part of the health department.

1. Administrative and field methods requiring special effort directed toward selected individuals.

(*a*) Investigation of sexual, family, and suspected contacts.

(*b*) Follow-up of previously treated syphilitic patients who lapsed from treatment and routine follow-up, did not respond to a reminder post card, and re-

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[1] From the School of Public Health, University of North Carolina. These studies are supported jointly by grants from the International Health Division of the Rockefeller Foundation and the North Carolina State Board of Health.

[2] Presented at the Eleventh Annual Session of the American Venereal Disease Association, Washington, D. C., April 8, 1949.

Acknowledgment: The authors wish to express appreciation to the Superintendent of the Durham City and County Health Department and to the Director and staff of its Venereal Disease Clinic, whose cooperation made this study possible.

quired vigorous additional effort (a field visit or the use of legal measures) to bring them back to the clinic.

2. Educational methods directed toward either selected or unselected groups, resulting in voluntary application for diagnosis on the patient's initiative.

3. All other methods:

(*a*) Routine follow-up examination of persons previously treated, resulting in discovery of new cases through noting a rise in serologic titer, which led to further examination, or through the discovery of lesions which had escaped the patient's notice.

(*b*) Examination of persons suspected, due to circumstantial evidence, of having syphilis (jail inmates, "beer joint" habitues, etc.).

(*c*) Examination of military personnel whose disease was discovered by routine examination in the armed services at the time of induction into or separation from the service and who were then referred to the health department.

(*d*) Examinations required by law (premarital, prenatal, and for health certificates required by food handlers, domestic servants, beauticians, and barbers).

Analysis of Data

The data were classified and tabulated by case-finding method according to the following characteristics:

1. Sex.
2. Time lapse since last treatment.
3. Duration of lesion.
4. Agency of previous treatment.
5. Comparison of case-finding methods at time of previous and present diagnoses.

In the tables which present the data, the percentages do not add up to precisely 100 percent in some instances; these differences in summation are due to rounding. The Chi square goodness of fit was used to test the statistical significance of the data.[3]

Results of Study

A total of 142 cases of syphilis which met the criteria established for this study were observed among 127 individuals. Among males, 63 cases were seen in 57 individuals, of whom 6 had two separate episodes of syphilis in the period studied. Among females, 79 cases were found in 70 individuals, of whom 7 had two separate episodes of syphilis and one had 3 during the period studied.

There were 50 additional cases of infectious syphilis, reinfection or relapse, that were omitted either because there were no lesions visible to the patient or because reliable information regarding the case-finding procedure was not available.

Table 1.—*Number and percentage of cases,*[1] *by sex and case-finding method*

Case-finding method	Total		Male		Female	
	Number	Percent	Number	Percent	Number	Percent
Methods involving special effort:						
Contact investigation	41	28.9	14	22.2	27	34.2
Vigorous follow-up of lapsed cases	22	15.5	10	15.9	12	15.2
Patient's initiative	59	41.5	36	57.1	23	29.1
All other methods	20	14.1	3	4.8	17	21.5
Total	142	100.0	63	100.0	79	100.0

[1] Negro cases with previous history of diagnosis and treatment of syphilis, current diagnosis of primary or secondary syphilis (reinfection or infectious relapse), and lesion visible to patient.

Summary of Case-Finding Methods

As shown in table 1, out of the total of 142 cases, contact investigation brought 41 cases to diagnosis, and the follow-up of lapsed patients located 22; thus, administrative and field methods requiring special effort brought 63 cases

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[3] Grateful acknowledgment is made to the Institute of Statistics, Greater University of North Carolina, for assistance in this phase of the analysis.

(44.4 percent) to diagnosis. Educational methods resulting in finding the case through the patient's initiative brought 59 cases (41.5 percent) to diagnosis. All other methods were responsible for locating only 20 cases (14.1 percent).

Analysis of Case-Finding Methods by Sex

Table 1 and figure 1 show the case-finding methods by sex. Out of the whole group of 63 male cases, the contact-tracing procedure brought 14 to diagnosis, and the vigorous follow-up of lapsed patients located 10; thus, administrative and field efforts directed toward selected individuals brought 24 cases (38.1 percent) to recognition. Educational methods resulting in the patient seeking treatment were responsible for finding 36 cases (57.1 percent). All other methods brought 3 cases (4.8 percent) to diagnosis.

The female cases present a somewhat different picture. Out of the entire group of 79 cases, contact investigation brought 27 cases to the clinic and the follow-up of lapsed cases brought 12, a total of 39 cases (49.4 percent). The patient's initiative brought 23 cases (29.1 percent) to attention. All other methods were responsible for locating 17 cases (21.5 percent): the primary factor involved in this group was routine screening examination to satisfy legal requirements (food handlers, premarital, and prenatal).

Special attention is drawn to the difference between males and females in the relative effectiveness of the major case-finding measures. Administrative and field efforts directed toward selected individuals were responsible for bringing to attention virtually half of the female cases and almost two-fifths of the male cases. Whereas over half the male cases came to diagnosis through the patient's initiative, the proportion of females in this classification was much smaller, being roughly 30 percent.

The distribution of case-finding methods described in this section was significantly different from that which would have occurred by chance alone.

Analysis of Case-Finding Methods by Time Interval Since Last Treatment

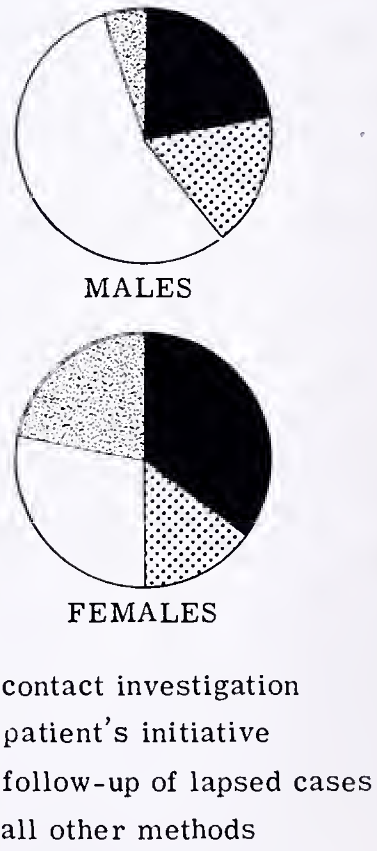
Table 2 presents the data, by sex, according to the length of time since the last treatment was received for syphilis prior to the present episode. The cases were classified into four groups, based on the date of the last treatment prior to the present episode: (1) less than 1 year, (2) 1 year or more but less than 2 years, (3) 2 years or more, and (4) unknown.

The available data do not appear to follow any decisive pattern, and the distribution of case-finding methods was not found to be statistically significant.

Figure 1

CASE-FINDING METHODS IN INFECTIOUS SYPHILIS BY SEX - NEGRO

Reinfection or Relapse



Analysis of Case-Finding Methods by Duration of Lesions

Table 3 presents the data, by sex, according to the duration of the visible syphilitic lesions before diagnosis. The cases with syphilitic lesions visible were classified into four groups: (1) less than 2 weeks, (2) from 2 through 3 weeks, (3) 4 weeks or more, and (4) unknown.

Again there is no clearly discernible pattern, and the distribution of case-finding methods was not significant statistically.

Table 2.—***Time lapse since last treatment of previous episodes,[1] by sex and case-finding method***

[Number and percentage]

Case-finding method	Time lapse since last treatment of previous case															
	Less than 1 year				1 to 2 years				2 years or more				Unknown			
	Male		Female		Male		Female		Male		Female		Male		Female	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Methods involving special effort:																
Contact investigation	8	20.0	7	18.4	5	41.7	12	54.5	1	11.1	7	41.2	0	0	1	50
Vigorous follow-up of lapsed cases	8	20.0	9	23.7	2	16.7	3	13.6	0	0	0	0	0	0	0	0
Patient's initiative	22	55.0	13	34.2	4	33.3	4	18.2	8	88.9	5	29.4	2	100	1	50
All other methods	2	5.0	9	23.7	1	8.3	3	13.6	0	0	5	29.4	0	0	0	0
Total	40	100.0	38	100.0	12	100.0	22	100.0	9	100.0	17	100.0	2	100	2	100

[1] Negro cases with history of previous diagnosis and treatment of syphilis, current diagnosis of primary or secondary syphilis (reinfection or infectious relapse), and lesion visible to patient.

Table 3.—***Length of time lesion was visible to patient before diagnosis,[1] by sex and case-finding method***

[Number and percentage]

Case-finding method	Length of time lesion was visible to patient before diagnosis															
	Less than 2 weeks				2 through 3 weeks				4 weeks or more				Unknown			
	Male		Female		Male		Female		Male		Female		Male		Female	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Methods involving special effort:																
Contact investigation	4	15.4	8	40.0	3	20.0	3	17.6	4	33.3	11	47.8	3	30.0	5	26.3
Vigorous follow-up of lapsed cases	6	23.1	4	20	3	20	3	17.6	0	0	1	4.3	1	10	4	21.0
Patient's initiative	16	61.5	7	35	8	53.3	8	47.0	8	66.6	5	21.7	4	40	3	15.8
All other methods	0	0	1	5	1	6.7	3	17.6	0	0	6	26.1	2	20	7	36.8
Total	26	100.0	20	100.0	15	100.0	17	100.0	12	100.0	23	100.0	10	100.0	19	100.0

[1] Negro cases with history of previous diagnosis and treatment of syphilis, current diagnosis of primary or secondary syphilis (reinfection or infectious relapse), and lesion visible to patient.

Analysis of Case-Finding Methods by Agency of Previous Treatment

Table 4 presents the data, by sex, according to the agency of former treatment (rapid treatment center, armed services, public health clinic, private physician, and other). There is no clearly demonstrated pattern, and the distribution of case-finding methods was not significant statistically.

Comparison of Case-Finding Methods at Time of Previous and Present Diagnoses

Reliable information was available regarding the case-finding mechanism involved in bringing the case to recognition at the time of the previous diagnosis in 88 out of the 142 cases considered in this study. These data, presented in table 5, represent 36 male and 52 female

Table 4.—*Agency which treated previous episode,*[1] *by sex and case-finding method*

[Number and percentage]

Case-finding method	Agency which treated previous case															
	Rapid treatment center				Armed services				Health department				Private physician and other			
	Male		Female		Male		Female		Male		Female		Male		Female	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Methods involving special effort:																
Contact investigation	7	21.9	18	37.5	4	28.6	0	0	1	8.3	8	32.0	2	40.0	1	16.7
Vigorous follow-up of lapsed cases	9	28.1	12	25.0	0	0	0	0	1	8.3	0	0	0	0.0	0	0
Patient's initiative	15	46.9	10	20.8	9	64.3	0	0	9	75.0	11	44.0	3	60.0	2	33.3
All other methods	1	3.1	8	16.7	1	7.1	0	0	1	8.3	6	24.0	0	0.0	3	50.0
Total	32	100.0	48	100.0	14	100.0	0	0	12	100.0	25	100	5	100	6	100.0

[1] Negro cases with history of previous diagnosis and treatment of syphilis, current diagnosis of primary or secondary syphilis (reinfection or infectious relapse), and lesion visible to patient.

Table 5.—*Comparison of case-finding methods at time of previous and present diagnoses* [1]

[Number and percentage]

At time of previous diagnosis			At time of present diagnosis							
Case-finding method	Number	Percent	Contact investigation		Vigorous follow-up of lapsed cases		Patient's initiative		All other methods	
			Number	Percent	Number	Percent	Number	Percent	Number	Percent
Methods involving special effort:										
Contact investigation	33	37.5	17		11		3		2	
Vigorous follow-up of lapsed cases	3	3.4	0		1		1		1	
Patient's initiative	32	36.4	7		5		17		3	
All other methods	20	22.7	6		4		6		4	
Total	88	100	30	34.1	21	23.9	27	30.7	10	11.4

[1] Negro cases with history of previous diagnosis and treatment of syphilis, current diagnosis of primary or secondary syphilis (reinfection or infectious relapse), and lesion visible to patient.

cases. Because of the essential similarity of the data for both sexes, they are presented in a combined table. The number of cases which came to diagnosis through the patient's initiative decreased from 32 at the time of the previous diagnosis to 27 at the time of the present episode. Actually, only 17 of the original group of 32 cases that came to diagnosis through the patient's initiative did so again at the time of the subsequent appearance of syphilitic lesions. However, 10 cases which had previously been brought to diagnosis by other methods now came to attention through the patient's initiative. On the other hand, contact investigation and follow-up of lapsed cases, which had previously brought only 36 cases to treatment, located 51 cases in the present episode.

Discussion

In determining the relative effectiveness of the various case-finding technics, as demonstrated by the experience of health departments, special attention must be paid to the role of technics involving administrative or field effort directed toward selected individuals. These technics are considered more difficult to practice than routine and miscellaneous case-finding measures, such as serologic testing and educational programs. Having analyzed the experience of two health departments so far as newly discovered cases of syphilis were concerned, it was believed that it might be interesting and valuable to analyze a series of "repeaters" on a similar basis.

The 142 cases studied in this report had all received some treatment for syphilis previous to the occasion on which a diagnosis of primary or secondary syphilis, either reinfection or relapse, was made. Furthermore, each had one or more syphilitic lesions within his own range of vision. Informing a person of a diagnosis of syphilis is in itself an educational procedure of some importance which, at a very minimum, is accompanied by some statements about the disease and the enunciation of a few rules for the patient's future behavior. As seen in table 4, 131 cases (92.2 percent of the total) had been previously treated in the armed services, in rapid treatment centers, or in health department clinics. These agencies have specially designed educational programs for their patients, in which, among other things, the recognition of syphilitic lesions is discussed and the need for immediate diagnosis of suspicious lesions is stressed. On this basis, one might expect that the majority of the cases studied would have come to diagnosis through the initiative of the patient, since each has been taught to recognize syphilis as a possible cause of his visible, suspicious lesion.

Analysis of our data indicates, however, that such an expectation is not justified by our experience, since only 41.5 percent of the cases came in through the patient's initiative. Thus, the proportion of "repeater" cases that came to attention through the patient's initiative was virtually the same as the proportion (42.1 percent) of first episodes of infectious syphilis among Negroes that came in through the patient's initiative in the study reported previously (*1*). In the former study, also, it was found that contact investigation brought in 38.4 percent of the first episodes of infectious syphilis. This is to be compared with the fact that, in the group of "repeaters" analyzed in this report, contact investigation brought in 28.9 percent and the follow-up of lapsed cases brought in 15.5 percent, thus making a total of 44.4 percent located as a result of special efforts directed toward selected individuals. This is illustrated graphically in figure 2.

There is an interesting difference between the sexes in the effectiveness of case-finding methods. The patient's own initiative brought to diagnosis 57.1 percent of the male cases as compared with only 29.1 percent of the female cases. This is particularly interesting because each of these patients had a lesion visible to himself. This suggests that education aimed at raising the "level of suspicion" of the lay person as to the possibility of his lesion being due to syphilis was either not reaching females to the same degree as males, or that females have a greater tendency to ascribe visible suspicious lesions to causes other than venereal disease.

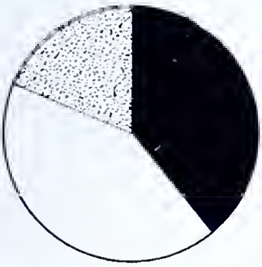
The data available in this analysis of cases of multiple episodes of infectious syphilis did not indicate any definite pattern of correlation between the various case-finding measures and such factors as the time interval since last treatment, the duration of the visible lesion, and the agency of previous treatment.

Reliable records indicating the case-finding method at the time of the previous diagnosis made possible a study of this factor in 88 cases (62 percent of the whole group). These data indicate that the patients who originally came to diagnosis on their own initiative could not be counted on to do so in subsequent episodes, since only 17 out of the original 32 came to diagnosis voluntarily in their later episodes. Furthermore, special efforts directed toward selected individuals (contact investigation and follow-up of lapsed cases) brought in a greater number of cases at the time of subsequent infection than on the occasion of the previous infection.

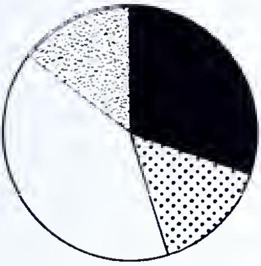
Figure 2

CASE-FINDING METHODS IN INFECTIOUS SYPHILIS

NEGRO



FIRST EPISODES
(951 Cases)



REINFECTIONS and RELAPSES
(142 Cases)

These data seem to indicate quite strongly that, if special efforts in contact tracing and the follow-up of lapsed cases had been relaxed in the health department and reliance placed mainly upon the educational effect of previous treatment and its accompanying educational program, many of the cases of multiple episodes of infectious syphilis would have come to attention and control later than they did, if at all. It may be, of course, that syphilitic reinfection usually occurs in persons with a low receptivity to education. This explanation, however, would not apply to cases of relapse.

Conclusions

1. Accurate information on the relative effectiveness of the major case-finding measures in the discovery of cases of syphilitic relapse and reinfection is essential for the development and maintenance of an adequate syphilis control program. Such knowledge can be obtained by a careful analysis of the data relating to the case-finding methods which bring these cases to diagnosis.

2. This analysis of 142 Negro cases of primary or secondary syphilis (either reinfection or infectious relapse) covered a 4-year period in an urban health department in the southern United States and indicated that, in such cases:

(*a*) Special field efforts (contact investigation and active follow-up of lapsed cases) were responsible for bringing under control 44.4 percent of the cases, while the patient's initiative was responsible for 41.5 percent.

(*b*) Special field efforts were most effective in the female cases, being responsible for bringing to diagnosis 49.4 percent of the total female group.

(*c*) In the male cases, the educational process, as evidenced by the proportion of cases which came in due to the patient's initiative, was the most important case-finding measure, being responsible for bringing to diagnosis 57.1 percent of the cases. Special field efforts were responsible for locating 38.1 percent.

(*d*) The fact that a patient came to diagnosis on his own initiative at the time of the previous syphilitic episode is not a reliable indication that he will again come to diagnosis on his own initiative when the lesions of a subsequent episode appear.

3. In terms of the relative effectiveness of various case-finding measures, the problem of discovering and bringing under control those individuals who have multiple episodes of infectious syphilis is essentially the same as that of discovering first infections.

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Serologic Activity of Dipalmityl Lecithin

Preliminary Report

Arthur A. Rosenberg, Serologist, United States Public Health Service [1]

Purified lecithin (*1*) is a component of cardiolipin antigens used in tests for syphilis, since cardiolipin alone or in combination with cholesterol has little or no active antigenic qualities. This "purified lecithin" is a compound or a mixture of compounds of differing unsaturated fatty acid composition (*2*). The difficulty of isolating and purifying such a substance to constant serologic reactivity is evident. For this reason, an investigation was undertaken to determine the serologic reactivity of a lecithin (dipalmityl) of constant fatty acid composition.

Dipalmityl lecithin was isolated from beef lung tissue in accordance with a method described by Thannhauser (*3*). Antigens were prepared with this substance and cardiolipin in concentrations recommended for complement-fixation and flocculation procedures. The antigen formulas are presented in table 1.

Table 1.—*Concentration of antigen components*

	Kolmer complement-fixation test (*4*)	VDRL slide test (*5*)
	Percent	*Percent*
Cardiolipin	0.03	0.03
Dipalmityl lecithin	.05	.20
Cholesterol	.60	.90

Antigens listed in table 1 were used in parallel with similar antigens containing purified lecithin for testing individual serums. The results of these tests are recorded in table 2. The serologic reactions obtained indicate that dipalmityl lecithin is an effective antigenic component for the sensitization of serologic antigens used in tests for syphilis. No attempt was made to adjust the concentration ratios of dipalmityl lecithin, cardiolipin, and cholesterol in order to correct for the difference in reactivity level observed.

Discussion

Adequate criteria of purity for lecithin used as a serologic reagent are difficult to

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[1] From the Venereal Disease Research Laboratory, U. S. Marine Hospital, Staten Island 4, N. Y., Medical Director J. F. Mahoney in charge.

Table 2.—*Comparison of tests performed with antigens containing dipalmityl lecithin and antigens containing purified lecithin*

Specimen	VDRL slide flocculation test		Kolmer complement-fixation test	
	Antigen with purified lecithin	Antigen with dipalmityl lecithin	Antigen with purified lecithin	Antigen with dipalmityl lecithin
1	Negative	Negative	Negative	Negative
2	Positive	Positive	Positive	Positive
3	Weakly positive	Weakly positive	Positive	Negative
4	Negative	Negative	Negative	Negative
5	Negative	Negative	Negative	Negative
6	Negative	Negative	Positive	Doubtful
7	Weakly positive	Weakly positive	Positive	Positive
8	Weakly positive	Weakly positive	Positive	Doubtful
9	Positive	Weakly positive	Positive	Positive
10	Positive	Positive	Positive	Positive
11	Negative	Negative	Negative	Negative
12	Positive	Positive	Positive	Positive

establish. For this reason, standardization of cardiolipin-lecithin antigens is usually accomplished by varying the lecithin content (*4, 5, 6, 7, 8, 9*).

The chemical structure of dipalmityl lecithin is a known constant. With dipalmityl lecithin as an antigen component, standardization of cardiolipin antigens should be simplified, since the serologic reactivity of this compound should be predictable on the basis of dry weight. The use of a more reproducible lecithin should also reduce the differences in test results attributable to the chemical variability of any portion of the lecithin molecule.

The difficulties associated with the production of antigenic substances in pure form are well known. Ideally, the most satisfactory serologic antigen would be one whose components can be synthesized. In this regard it is interesting to note that L-α-dipalmityl lecithin has been synthesized by Dr. Erich Baer (*10*) of Banting Institute. Cardiolipin antigens prepared with this synthetic lecithin (Hinton (*6*), Kline (*7*), Kolmer (*4*), Rein-Bossak (*9*), VDRL (*5, 11, 12*)) reacted antigenically. However, the small quantity of synthetic dipalmityl lecithin, graciously made available to this laboratory by Dr. Baer, did not permit accurate standardization of each of these antigens.

Conclusion

Dipalmityl lecithin is an effective antigen component in combination with cardiolipin for use in serologic tests for syphilis.

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Mass Public Venereal Disease Education—Ohio Fairs

Charles R. Freeble, Jr., M. D.;[1] Earl O. Wright, Health Program Representative;[2] and Robert S. Bogue[3]

In a project sponsored by the Ohio Department of Health in 1948, venereal disease education invaded the midway at eight county fairs and one State fair, attracting 119,783 persons. The health department has become increasingly aware of the demand on the part of the public for education concerning venereal diseases. This eagerness for information in Ohio, which has been previously reported,[4] has been so great that in many cases it has far surpassed our ability to fulfill the demand.

We are primarily interested in making the information available because we feel that, in so doing, we can alter public attitudes toward venereal disease in such a manner that a number of the problems in the field of venereal disease control can be directly attacked. If people can be made to realize that syphilis, regardless of the moral implications of its chief means of infection, transmission, and spread, is a serious and widespread disease which affects them directly as parents, citizens, and taxpayers, perhaps they will awaken from their lethargy and take action against the contributing social conditions which can exist only so long as they are tolerated. A better-informed public should also result in more persons presenting themselves for early diagnosis and treatment, less reticence because of fear of ostracism or loss of employment, and less reluctance to submit to routine diagnostic tests. By the same token, uninformed opponents of venereal disease control must be made to realize that early diagnosis and treatment is much cheaper and more sensible than the expensive care of late complications, disregarding the huge toll in human health and suffering.

In giving venereal disease information to the public, the health department feels that more can be accomplished by supplying a small amount of sound factual material to great masses of the population than by the more conventional method of providing a greater amount of education to small selected groups. The various county fairs held in Ohio during the fall of 1948, followed by the huge Ohio State Fair, appeared to present an excellent opportunity for the dissemination of venereal disease information.

The Ohio Department of Health decided to offer a tent show to the fair boards of eight counties as well as to the State fair board. The members of the boards were enthusiastic about the idea and immediately offered to reserve space on their midways for the exhibit and to assist in any other practical way. Since crowds at fairs are entertainment bent, it was obvious from the start that the tent show should have distinct appeal in order to compete with other attractions along the midway. Through the courtesy of civic-minded local businessmen, the free services of commercial artists were secured and an attractive, eye-catching display was designed for presenting in good taste the venereal disease story.

A carnival tent, 30 by 60 feet, was rented for the season. A leading Columbus commercial artist was employed to build the displays in such a manner as to fold and pack easily, so that they might be readily transported from one fair to another. Bright and cheerful colors were used wherever possible. Fear technic was avoided and stress was placed on giving information. Photographs and sketches were used to reduce the printed word to a minimum.

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[1] Chief, Venereal Disease Division, Ohio Department of Health; John D. Porterfield, M. D., Director.

[2] U. S. Public Health Service.

[3] Coordinator, Venereal Disease Division, Ohio Department of Health.

[4] Freeble, C. R., Jr.; Robinson, A.: The tabloid newspaper as a medium of mass public venereal disease education. J. Ven. Dis. Inform., 29: 307–312, 1948.

A departure from the usual type of health exhibit was the use of papier-mâché figurines in three-dimensional displays to illustrate such items as the nature of the spread of syphilis and the complications of the disease. United States Public Health Service posters, as well as a number of original posters, were placed on the display panels. The tent, with a capacity for seating 65 persons in the center, was used to show venereal disease training films. The display panels lined the sides and the entrance. The training films "Know for Sure" (revised version) and "Message to Women" were shown alternately. Between shows the members of the audience looked at the displays and selected any of the standard venereal disease literature that interested them.

The outside of the tent was identified by a simple sign which read, "Sponsored by Your Local Health Department in Cooperation with the Ohio Department of Health, Venereal Disease Division." A canvas fly was hung above and at the sides of the entrance. The words "Free Movies" appeared in bold letters. On one side of the fly, a healthy, happy young man was painted, and on the other side the same man appeared, sad and obviously ill.

With no other ballyhoo than this, the show was able to compete favorably with any other tent on the midway and played to standing audiences at each fair. Personnel were not available to conduct a count of the exhibit audience at any of the 9 fairs, but a house count immediately after each showing of the movies gives the approximate number attending the exhibit at each fair. The number of persons who failed to stay through a complete showing of the movies or who stepped inside merely to look at the displays or to obtain some of the free literature could not be estimated. Out of 745,000 who attended these fairs, we estimate that 119,783 persons attended the exhibit long enough to see at least one movie. The official attendance figures released by the State Fair Board for the fairs concerned and the attendance at the venereal disease exhibits are listed in table 1. The exhibit audience of 119,783 persons constituted 16.1 percent of the total admissions to the 9 fairs. The lowest attendance ratio (9.9 percent) occurred at the Champaign County Fair and was attributed to the fact that the tent was located some distance from the midway. Hancock County, the smallest fair visited, yielded the highest attendance ratio (57.3 percent).

Table 1.—*Attendance at the venereal disease exhibits compared to total attendance at Ohio fairs, 1948*

Fair	Date of fair	Total attendance [1] at fair	Estimated attendance at exhibit	Percentage of total who attended exhibit
Chippewa Lake	Aug. 4–6	25,000	6,450	25.8
Champaign County.	Aug. 10–14	90,000	8,900	9.9
Cuyahoga County	Aug. 17–22	79,000	10,640	13.5
Ohio State Fair	Aug. 28–Sept. 3.	392,000	44,483	11.3
Hancock County	Sept. 8–11	15,000	8,600	57.3
Pickaway County	Sept. 14–18	20,000	5,240	26.2
Hardin County	Sept. 28–Oct. 1.	20,000	7,655	38.3
Coshocton County.	Oct. 5–9	34,000	14,450	42.5
Fairfield County	Oct. 12–16	70,000	13,365	19.1
Total		745,000	119,783	16.1

[1] Number of persons attending fairs (to the nearest thousand) officially released by the Ohio State Fair Board.

Quantities of the various educational pamphlets were placed on a shelf, over which was a panel displaying sample copies and the words, "This is Your Information." Conveniently located near the entrance, the display was passed by the audience upon entering and leaving the tent. People selected pamphlets of their choice, and many persons who did not care to see the movies or who were unable to do so because of the crowded tent selected literature before leaving. In this manner, 122,300 pieces of literature (all the available supply) were distributed. A careful check was made of the littered fairgrounds and only at one fair were venereal disease pamphlets found in the rubble. This indicates to us that the literature was being taken home, where a large number of additional people may have read the pamphlets.

Much of the success is attributed to the open and casual manner with which the audience was treated. They were not asked to fill out questionnaires, they were not lectured to, and no restrictions were placed on age, sex, or color. A responsible person was present to answer all but strictly medical questions, and any person asking medical questions was referred to his local health commissioner. In no known instance did the exhibit receive unfavorable criticism. The following remarks by a lady in the audience set the general tone for the comments which were overheard: "I'm an old lady. I won't say how old, but this is the first one of these shows I've ever seen, and I want to tell you what a wonderful thing it is. Young people deserve the chance to lead clean lives, helped by information like this." A man whose son had contracted syphilis while serving in the armed forces said, "My wife and I have been very much interested in finding out ways in which we, as citizens, can do something to help prevent the spread of this dreadful disease."

Of special interest was the manner in which the exhibit was greeted by the carnival people. At four of the fairs, at the request of the carnival workers, special showings were made in the early morning hours, after closing time, and these were attended by overflow audiences. One of the men said, "We have been running a stand at this fair for 17 years and this is the first time we have ever seen anything like this health exhibit. It's good to have you here. You should have exhibits at all fairs. We want one of each of these pamphlets to send to our daughter—she's in college now."

Also of interest was the way in which organizations ranging from women's religious clubs to Boy Scout troops attended as a body and went away favorably impressed.

The entire exhibit cost $7,518.11, which means that venereal disease education was made available to 119,783 persons for 6 cents each. Table 2 presents the breakdown of expenses. The largest single item is salaries, but this includes salaries paid to workers from May 1, 1948, when the project entered the planning stage, through October 16, 1948, when the last fair closed. The Division of Venereal Disease of the United States Public Health Service cooperated by lending us a truck, which made it possible to move the exhibit from fair to fair in rapid succession.

Table 2.—*Expenditures for venereal disease exhibits at Ohio fairs, 1948*

Item	Cost	Percentage of total cost
Salaries	$2,640.06	35.1
Literature	2,500 00	33.3
Exhibit construction	944.73	12.6
Tent rental	780.00	10.4
Electrical equipment	364.76	4.8
Travel expenses	181.31	2.4
Chair rental	55.00	.7
Gasoline	40.00	.5
Miscellaneous	12.25	.2
Total	$7,518.11	100.0

The Venereal Disease Division has received requests from 11 other counties asking for the exhibit at their fairs next season and meanwhile is lending parts of the exhibit to various health departments for use in group meetings in local areas. Taking the admonition of the small town minister who said, "Why did it take you so long to get this program operating at fairs? You should have started this years ago," the Ohio Department of Health is planning on having a better exhibit on the road next season.

In summary, we believe that an effective demonstration of mass public health education has been completed; that the technic and approach used can be adapted to public health problems other than venereal disease; and that such a program carefully planned and effectively presented will be enthusiastically received by the fairgoing public anywhere.

CURRENT NOTES AND REPORTS

Middletown's VD Campaign a Success

A report from Dr. L. C. Neer, Health Commissioner for the city of Middletown, Ohio, outlines the success of the venereal disease educational and case-finding drive recently completed in that city.

For a 7-week period the spotlight was focused on gonorrhea and syphilis in an attempt to inform the public regarding these diseases—the damage they cause, something of the symptoms, and the fact that penicillin offers a quick, painless, and economical cure.

The drive was built around the broadcasting of fourteen 15-minute radio transcriptions produced by Columbia University and the United States Public Health Service. Two programs were broadcast each week, and numerous spot announcements were used to call the attention of listeners to the programs. Station WPFB donated time on the air as a public service for the broadcasting of the series.

Taking advantage of the offer to provide free venereal disease literature, listeners throughout Ohio requested material. Many phone inquiries were received by our health department.

During the drive three articles were prepared for publication in the Middletown Journal, and the broadcasts were advertised. A brochure on social hygiene was prepared and distributed to all high-school teachers and clergymen in the city. Forty posters were supplied to industrial plants, and posters were displayed in the downtown section. Eleven thousand leaflets were distributed—one mailed to each home, place of business, and industrial plant in the city. Leaflets were also distributed to residents of hotels and rooming houses, taxi drivers, food handlers, and patrons of beer taverns. The venereal disease film "Plain Facts" was shown to 30 boys at Roosevelt Junior High School. Talks on venereal disease were given before the Kiwanis and Optimist Clubs.

Attendance at the two venereal disease clinics operated weekly by the health departments doubled during the following month. Clinic patients totaled 108, new patients were interviewed and accepted for treatment, and 40 blood samples were collected. Private physicians reported new cases.

It is believed the drive was a success and that the people of Middletown are at least partially venereal disease conscious.

A Psychiatric Approach to the Treatment of Promiscuity

An 88-page report entitled "A Psychiatric Approach to the Treatment of Promiscuity," setting forth the results of the application of psychiatric knowledge and technics to the field of venereal disease control, is to be published in 1949 by the American Social Hygiene Association. This report is a further development and an expansion of an earlier study, published in 1945, entitled "An Experiment in the Psychiatric Treatment of Promiscuous Girls." Both projects were carried out under the auspices of the Division of Venereal Disease, United States Public Health Service, the California State Department of Public Health, and the San Francisco Department of Public Health.

The publication should prove useful to physicians, nurses, and social workers. In addition to the medical and public health values of the study, it contains important information on social, educational, and community welfare problems arising from the sexual behavior of both men and women. The logically arranged chapters, containing illustrative cases which add interest and clarity to the text, lead convincingly to conclusions and recommendations which should stimulate community action toward preventive social hygiene measures.

The study is based on the voluntary attendance of 365 women and 255 men at the Psychiatric Service of the San Francisco City Clinic over the period January 1943 to July 1947. In attempting to determine the factors motivating promiscuity and the value of psychiatric treatment in reducing promiscuity, a comprehensive study was made of the personal and social factors affecting each patient. While no single factor or group of factors could be ascertained which would either determine or exclude promiscuity, such unsatisfactory familial relationships as broken homes were found to be among the factors having a direct relationship to promiscuous behavior. Sex instruction in this group had usually been inadequate, and sex conflicts were many. Emotional and social immaturity, instability of character, neuropsychiatric behavior, and neurotic tendencies were seen frequently. Promiscuity appeared in most cases to be symptomatic behavior arising out of neurotic conflict, with such environmental factors as unsatisfactory living conditions and the absence of community ties seen as contributing causes.

A study of the modification of promiscuity in habitually promiscuous persons was made. Of 208 promiscuous women and 149 promiscuous men, 67 percent and 76 percent, respectively, were classified as habitually promiscuous. With few exceptions, habitual promiscuity was found to be the result of difficulties within the personality—conflicts, inadequacies, or other types of disturbance. Lack of social responsibility and self-restraint were also frequent findings.

Follow-up at 6 months and in many cases at 12 months or more revealed dramatic improvement in most instances. Of the 68 percent for whom follow-up data were completed, 88 percent had reduced their promiscuity (or if potentially promiscuous, had not become promiscuous); within the follow-up period, one-half of these patients had ceased to have extramarital relationships.

Recommendations based on the study include general education measures, such as preparation for marriage and guidance to parents regarding sex instruction of their children, and special services, such as adequate family service and mental hygiene facilities to detect emotional disturbances in children. The necessity for complete correlation between medical, social, and moral activities in the field of public welfare is pointed out.

The Psychiatric Service of the San Francisco City Clinic has demonstrated that psychiatric facilities in connection with a venereal disease clinic can offer treatment which not only results in reduction or elimination of promiscuity among patients who voluntarily utilize the Service but also promotes the two objectives of venereal disease control and mental hygiene.

This report (Publication No. A-741) may be obtained from the American Social Hygiene Association, 1790 Broadway, New York 19, N. Y.

CURRENT LITERATURE

NOTE: Abstracts of any article listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

AM J. PUB. HEALTH, NEW YORK

- A new national health program for Canada. [Venereal disease control.] G. D. W. Cameron. 38: 1643–1652, Dec. 1948.
- Penicillin or silver nitrate as a prophylactic against ophthalmia neonatorum? Conrad Berens and Franklin M. Foote. 38: 1680–1682, Dec. 1948.

AM. J. SYPH., GONOR. & VEN. DIS., ST. LOUIS

- *Penicillin syphilotherapy administered prior to pregnancy. A study of 111 pregnancies during which additional antisyphilitic treatment was withheld. Harold A. Tucker. 33: 1–7, Jan. 1949.
- *The therapeutic efficacy of penicillin G in experimental syphilis produced by five different strains of *Treponema pallidum*. Ruth A. Boak and Charles M. Carpenter. 33: 8–11, Jan. 1949.
- *Results of the nationwide study of penicillin in early syphilis. A report of the Central Statistical Unit. I. Amorphous penicillin in aqueous solution. Margaret Merrell. 33: 12–18, Jan. 1949.
- *Results of the nationwide study of penicillin in early syphilis. II. Amorphous penicillin versus crystalline penicillin G, and aqueous penicillin versus penicillin-oil-beeswax. Rowland V. Rider. 33: 19–26, Jan. 1949.
- Observations on patients with early syphilis treated with penicillin in various vehicles and by oral method. Alfred Cohn, Theodore Rosenthal and Isaak Grunstein. 33: 27–33, Jan. 1949.
- Osteomyelitis of the skull in early syphilis. Report of two cases probably influenced by trauma. Robert G. Thompson, Charles L. Leedham and Howard Hailey. 33: 34–42, Jan. 1949.
- *Cardiovascular syphilis. A summary of recent information with special reference to treatment with penicillin. Joseph Earle Moore. 33: 43–55, Jan. 1949.
- Extradural hemorrhage following lumbar puncture: Report of a case. Sidney Olansky. 33: 56–57, Jan. 1949.
- Streptomycin therapy in a case of sulfonamide-resistant *Hemophilus ducreyi* (chancroid) infection. W. D. Weber, J. H. Williams and T. R. Huffines. 33: 58–59, Jan. 1949.

Penicillin syphilotherapy administered prior to pregnancy. A study of 111 pregnancies during which additional antisyphilitic treatment was withheld. Harold A. Tucker. Am. J. Syph., Gonor. & Ven. Dis., 33: 1–7, 1949.

This study was made in an effort to determine whether or not penicillin is required during each pregnancy in women previously treated for syphilis. Between 1944 and 1948, 88 women with penicillin-treated early syphilis were permitted to go through one or more subsequent pregnancies without additional antisyphilitic treatment. In 72 of these patients, the original diagnosis had been primary or secondary syphilis and in the remainder, early latent or early asymptomatic neurosyphilis. With one exception, all were given aqueous penicillin intramuscularly every 2 or 3 hours for 7½ to 15 days. Of these 88 women, 34 had been treated during a previous pregnancy, while 54 had been treated while nonpregnant. Both groups were followed, and as soon as a diagnosis of pregnancy was established, they were registered in a special prenatal clinic where monthly examinations of the skin and mucous membranes were carried out, in addition to the usual routine of prenatal care. On each visit a titered serologic test for syphilis was performed. The presence of syphilitic mucocutaneous lesions of relapse, a confirmed rise in serologic titer, or a failure of the titer to fall in a satisfactory manner after therapy were considered reasons for immediate re-treatment. Re-treatment during pregnancy was indicated in 5 patients and carried out in 4.

Of the 111 pregnancies resulting in 101 live births, there were three premature infants and three neonatal deaths. Of 7 abortions and 3 stillbirths, none was thought to be due to the treated disease. One syphilitic infant occurred in this study from an uncooperative mother who had no serologic tests during the pregnancy.

It is concluded that amounts of penicillin in excess of 2.4 million units to which syphilitic pregnant or nonpregnant women have responded satisfactorily are sufficient to guarantee healthy offspring in subsequent pregnancies, provided that relapse or reinfection do not occur.

The therapeutic efficacy of penicillin G in experimental syphilis produced by five different strains of *Treponema pallidum*. Ruth A. Boak and Charles M. Carpenter. Am. J. Syph., Gonor. & Ven. Dis., 33: 8–11, 1949.

This study was undertaken to determine if a variation in the resistance of strains of *Treponema pallidum* to penicillin G might explain why the drug will not cure a greater percentage of patients with syphilis.

The five strains of *T. pallidum* employed in the experiment had been maintained by animal passage in rabbits for from 6 months to 34 years. The strains used were the Nichols, Zinsser-Hopkins, All, Ama, and Ami. The last three strains were isolated in recent years from penile chancres by the intratesticular inoculation of rabbits. Five groups of 10 rabbits each were inoculated intratesticularly with the five different strains of treponemes which had been well adapted to the rabbit. Approximately 6 weeks after inoculation, the animals developed typical lesions of experimental syphilis which were darkfield positive and were treated wtih a single lot of crystalline penicillin G. The penicillin was dissolved in an 0.85-percent solution of sodium chloride and frozen immediately in amounts required for each injection of the 50 rabbits. Each group of 10 rabbits received, per kilogram of body weight, a total dosage of either 500, 1,000, 2,000, 4,000, or 8,000 units. The penicillin was administered intramuscularly every 4 hours for 24 injections. During the next 6 months in which the rabbits were observed, darkfield examinations were made on any lesions suspicious of syphilis. The rabbits which did not show clinical evidence of syphilis were sacrificed at the end of the observation period and were tested for cure by transfer of suspensions of testes and of lymph nodes to rabbits with negative serologic tests for syphilis. The rabbits employed as tests for cure were kept under observation for 6 months. Samples of blood were collected at monthly intervals for serologic tests for syphilis. Whenever lesions developed, darkfield examinations were carried out. If the rabbit remained normal and the serologic tests negative, the original animal from which the tissues were obtained was designated as cured. If no lesions appeared, but the serologic test became positive, the animal was sacrificed and tested for cure by inoculating a second seronegative rabbit and similarly observing him.

It was found that the Nichols strain of *T. pallidum* required the greatest amount of penicillin per kilogram of body weight to effect a cure, the CD/50 being 2,520 units. The Zinsser-Hopkins strain was next with a CD/50 per kilogram of body weight being 1,570 units. The CD/50 for the All strain was 1,420 units per kilogram of body weight and 1,210 units for the Ama strain. Least resistant to penicillin was the Ami strain with the CD/50 being only 500 units.

The comparison of the sensitivity of the five strains showed a considerable variation. Neither the length of time that a strain had been maintained by animal passage in rabbits nor the number of passages appeared to be the significant factor responsible for the variation.

Results of the nationwide study of penicillin in early syphilis. A report of the Central Statistical Unit. I. Amorphous penicillin in aqueous solution. Margaret Merrell. Am. J. Syph., Gonor. & Ven. Dis., 33: 12–18, 1949.

This report was prepared in order to present certain issues on the Nation-wide study of early syphilis not incorporated in previous reports. One of these issues is the effect on failure rates of using more rigid criteria for designating a case as a treatment failure, while another concerns the effect on the failure rates of subclassifying cases as to stage of disease, sex, etc. For this study, failure rates are determined on clinical failures only, and any case is considered a success until reported as a clinical failure. As for the second issue, the cases are separated into three groups: Males with primary syphilis, males with secondary syphilis, and females with secondary syphilis. Approximately 7,000 cases are included in the analysis.

The failure rates are presented as cumulative rates from initiation of treatment, and rates are shown for all cases treated on seven different schedule groups ranging in a total dose of penicillin from 0.3 million units to 4.8 million units. At 15 months the rates range from 12 to 25 percent. The rates improve with increased dosage up to at least 1.2 million units. The highest rate is for 0.3 million units. It was found that the total failure rates determined on first failure, whether serologic or clinical, are approximately 1.5 times as large as the corresponding rates based on clinical failures only. Evidence indicates that when clinical failures alone are examined, at least 10 percent of the patients treated are classified as failures at the end of the first year on the most favorable of the amorphous-aqueous penicillin schedules.

When certain types of cases were compared, there were no significant differences at 15 months. In the group of males with primary syphilis, the rates ranged from 10 to 15 percent at 15 months when the corresponding rates for all cases ranged from 13 to nearly 20 percent. The clinical failure rates for males and females with secondary syphilis showed a definitely higher rate for the lower dose schedules. One explanation for this is that the small dose which might be adequate to deal with a new infection is inadequate to deal with a longer standing one.

From this study there is an indication that 2.4 million units has definite advantage over 1.2 million units.

Results of the nationwide study of penicillin in early syphilis. II. Amorphous penicillin versus crystalline penicillin G, and aqueous penicillin versus penicillin-oil-beeswax. Rowland V. Rider. Am. J. Syph., Gonor. & Ven. Dis., 33: 19–26, 1949.

This report is concerned with the specific comparisons of amorphous penicillin with crystalline penicillin G and of aqueous penicillin with penicillin-oil-beeswax. Most comparisons are based upon cumulative failure rates.

Of four schedules using crystalline penicillin G, two called for 2.4 million units to be given over a period of about 7.5 days, while the other two schedules called for 4.8 million units. Of the four schedules using 2.4 million units of amorphous penicillin, one using a peanut oil-beeswax medium was unsuitable for comparison because of insufficient follow-up. The other three amorphous schedules involved 3-hour intervals between injections and total durations of treatment of 4, 7.5, and 15 days. When clinical failures only were included, no very marked differences between the amorphous and the crystalline G appeared, but when serorelapses and seroresistants for whom clinical failure was not observed were included, there was a more marked difference between the two. One reason for this difference was the clinic differences on failure rates, and a larger proportion of clinics with poor follow-up were found among the amorphous clinics. These comparisons offer strong evidence that results obtained by crystalline G are superior to those obtained by amorphous penicillin up to the fourteenth month following treatment, when given in quantities of 2.4 or 4.8 million units over a 7.5-day period at the rate of one injection every 2 or 3 hours.

As for comparison of vehicles, an analysis of the reports received on the use of amorphous penicillin does not justify the conclusion that there is any difference between the cumulative failure rates obtained by the use of the peanut oil-beeswax vehicle and those observed among cases treated with penicillin in aqueous solution. At the fourteenth month no difference between the peanut oil-beeswax and the aqueous solution is detectable on the basis of cumulative failure rates.

In the over-all reaction rates there was no difference between the particular peanut oil-beeswax and aqueous schedules, except that there is some indication that abscesses at the point of injection were more common when peanut oil-beeswax was used. The incidence of Herxheimer reactions was about the same in each group.

Cardiovascular syphilis. A summary of recent information with special reference to treatment with penicillin. Joseph Earle Moore. Am. J. Syph., Gonor. & Ven. Dis., 33: 43–55, 1949.

The author reviews the contributions of the past decade relating to the incidence, early diagnosis, clinical course, and treatment of cardiovascular syphilis.

It is reasonably established that adequate treatment of early syphilis affords protection against the development of clinically recognizable cardiovascular syphilis. The campaign to control syphilis, which has brought so many patients with early and late syphilis under treatment in the past few years, will be reflected in a great decline in the incidence of cardiovascular syphilis in the next quarter century.

Many investigators have pointed out that the best hope of therapeutic success in cardiovascular syphilis lies largely in the recognition of aortic involvement before the development of valvular insufficiency or saccular aneurysm. Necropsy studies from many medical centers have confirmed the fact that from 80 to 90 percent of patients with long-standing syphilitic infections, inadequately treated during the early stages, show pathologic evidence of syphilitic aortitis. Available evidence indicates that in the hands of an experienced and duly suspicious observer, the clinical diagnosis of uncomplicated aortitis can be made successfully and accurately in a fair proportion of patients with this condition. Both syphilitic aortic insufficiency and aneurysm may frequently be present in clinically recognizable form for long periods before the development of symptoms.

Within the past 10 years a number of authors have reported findings on routine electrocardiograms performed on patients with syphilitic infections of varying duration, with and without clinical evidence of syphilitic heart disease, and before and after treatment. There are no characteristic electrocardiographic changes associated with syphilitic heart disease, as contrasted with other forms of heart disease; however, the electrocardiogram makes it possible to recognize the presence of involvement of one or both coronary ostia.

Whether and how to use penicillin in the treatment of cardiovascular syphilis is a problem. The harm, if any, is the Jarisch-Herxheimer reaction and the therapeutic paradox. It is the opinion of the author that the therapeutic paradox has been exaggerated, and there is no greater danger from it after penicillin than after arsenic and bismuth. The Herxheimer reaction is a more serious matter, but the author believes it essential to employ penicillin in the treatment of cardiovascular syphilis, at least on an investigative basis, in order to outline its risks and benefits.

ANN. DE DERMAT. ET SYPH., PARIS

Icterus in syphilitics treated with arsenobenzenes. Les ictéres des syphilitiques traités par les arsénobenzenes.) E. György. 11: 433, 1947. [Abstracted in Brit. J. Ven. Dis., London, 24: 164, Dec. 1948.]

ANN. SURG., PHILADELPHIA

*The results of the systemic administration of the antibiotic, bacitracin, in surgical infections. A preliminary report. Frank L. Meleney, William A. Altemeier, Alfred B. Longacre, Edwin J. Pulaski and Harold A. Zintel. 128: 714–731, Oct. 1948.

The results of the systemic administration of the antibiotic, bacitracin, in surgical infections. A preliminary report. Frank L. Meleney, William A. Altemeier, Alfred B. Longacre, Edwin J. Pulaski and Harold A. Zintel. Ann. Surg., 128: 714–731, 1948.

The authors report on a study of the results of the systemic administration of bacitracin in surgical infections. The results obtained in 105 patients are discussed extensively. Comparisons with other antibiotics are shown.

The chief advantages that bacitracin has over penicillin are: (1) it is not inhibited by the organisms which produce penicillinase and is, therefore, more likely to be effective in infections due to bacterial mixtures; (2) it is more slowly eliminated from the body; (3) its effectiveness against bacteria is in direct proportion to its concentration; and (4) so far, bacitracin has shown less tendency to produce allergic or hypersensitive reactions, but these may come with its more extended use. Its chief disadvantage is that it has not yet been obtained in a pure crystalline form and, in the present state of its impurity, it produces, when injected systemically in man, certain evidence of nephrotoxicity which limits its dosage and the duration of treatment.

As compared with streptomycin, the advantages of bacitracin are its wider antibacterial spectrum, particularly with regard to anaerobic organisms, and the low order of the development of resistance during the course of treatment.

More than 100 syphilis patients have been treated with bacitracin or a combination of bacitracin and penicillin by Eagle and his associates. Eagle has also demonstrated a significant synergistic action between penicillin and bacitracin in the treatment of experimental syphilis whereby small fractions of therapeutic doses of each, when combined, yield a therapeutic result.

Of the 105 cases of surgical infection reported in this study, the over-all response in about 70 percent of the cases was favorable. In the majority of the patients there was a transient albuminuria which disappeared either during continued treatment or soon after treatment was discontinued.

Specifications have been set up by the Food and Drug Administration for bacitracin which would permit its systemic use under experimental conditions and which would safeguard the patients during the course of its clinical appraisal. Some of the later preparations of bacitracin made by the deep tank method have shown evidence of nephrotoxicity. New specifications will have to be drawn up to detect these toxic factors.

The authors of this preliminary report are leaders of groups which are attempting to evaluate bacitracin in the systemic treatment of syphilis. These studies are being carried out with the aid of funds provided by the Medical Research and Development Board of the Surgeon General's Office and the Antibiotics Study Section of the National Institutes of Health.

ARCH. DERMAT. & SYPH., CHICAGO

- * Granuloma inguinale. A review of the literature and a report of ninety-seven cases, with a note on streptomycin therapy. Lydia Marshak, Robert L. Barton and Theodore J. Bauer. 57: 858–867, May 1948.
- * Ambulatory treatment of early syphilis. An experimental study with report of injection of penicillin in water-in-oil emulsion. Alfred Cohn, Theodore Rosenthal and Isaak Grunstein. 57: 900–906, May 1948.
- Penicillin therapy of yaws and serologic results. Charles R. Rein, Thomas H. Sternberg, James H. Dwinelle and Albert J. Sheldon. 57: 942–952, June 1948.
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- Treatment of early syphilis with penicillin in oil and wax. Albert Heyman. 58: 34–40, July 1948.

Granuloma inguinale. A review of the literature and a report of ninety-seven cases, with a note on streptomycin therapy. Lydia Marshak, Robert L. Barton and Theodore J. Bauer. Arch. Dermat. & Syph., 57: 858–867, 1948.

After a brief review of the literature, in which the increasing frequency of granuloma inguinale in the northern States is noted, the authors present a report on

97 patients with granuloma inguinale (96 Negro and 1 white) observed at the Chicago Intensive Treatment Center from October 1943 to November 1946. The diagnosis was confirmed by the presence of Donovan bodies in 79 patients and by clinical examination, biopsy studies, and response to antimony treatment in the other 18 patients. The duration of the disease, which varied from 1 week to 14 years, was generally reflected in the hemoglobin estimation, which was lower in those patients with a lengthy history of the disease.

Since out-patient treatment was unsatisfactory, all patients seen between March 1946 and November 1946 were hospitalized. Treatment consisted of intravenous administration of a 1-percent solution of antimony potassium tartrate. The dose ranged from 1 cc. to 10 cc., in ascending doses of 1 cc. per day until the maximum dose was reached, and then decreased by 1 cc. per day for the next 10 days. A course of treatment was considered to be a total of 100 cc. of antimony potassium tartrate. Of 25 patients thus treated, 21 responded favorably, 2 required another complete course of treatment, and 2 were considered failures. Such side effects as severe nausea, vomiting, and aching pains were occasionally observed when the drug was employed in a large dose (8 cc. to 10 cc.). Although antimony therapy was not completely discontinued in these patients, it was necessary to administer reduced doses at longer intervals, which considerably delayed the healing of the lesions.

Of 46 patients treated with antimony drugs and regularly observed, 5 (10.7 percent) failed to respond to this form of therapy. A case history is presented of one of these failures who subsequently was given streptomycin with striking results. The authors also give a case history of successful streptomycin treatment in a previously untreated patient.

In conclusion, the authors consider a 1-percent solution of antimony potassium tartrate effective when patients are hospitalized and treated regularly. Streptomycin, however, was also noted to be of outstanding value in the treatment of granuloma inguinale.

Ambulatory treatment of early syphilis. An experimental study with report of injection of penicillin in water-in-oil emulsion. Alfred Cohn, Theodore Rosenthal and Isaak Grunstein. Arch. Dermat. & Syph., 57: 900–906, 1948.

This report deals with various instructive observations recorded in the course of an experimental study of ambulatory treatment of early syphilitic patients with penicillin in water-in-oil emulsion. The group of 96 patients treated consisted of 16 with seronegative primary syphilis, 39 with seropositive primary syphilis, and 41 with secondary syphilis. In the case of 84 patients, 1 intramuscular injection was administered every 24 hours, while 12 patients received their daily dosage in 2 equally divided doses at 12-hour intervals. Total dosages of 2,000,000 units up to 5,000,000 units of sodium penicillin in water-in-oil emulsion were used. The daily dose varied from 400,000 to 1,000,000 units. The total treatment period of 83 patients was 5 days, while 13 patients were treated over a period of 10 days.

Before treatment was started all patients were examined both clinically by darkfield examination (with rare exceptions) and serologically. At the beginning, 56 patients were hospitalized for a period of 5 or 10 days, while later, ambulatory treatment was given to 40 patients.

Clinical results revealed complete healing of the primary lesions within an average period of 12.2 days and of the secondary lesions within an average period of 17.8 days. In 66 of the patients followed for a period of 3 to 26 months, 55 showed satisfactory clinical and serologic progress, 7 had infectious clinical relapse, and 2 had serologic relapse. The serums of 2 patients continued to present a positive Wassermann reaction.

The observations from this study, correlated with therapeutic results, indicate that the administration of penicillin in water-in-oil emulsion prolongs the presence and probably the therapeutic action of the antibiotic agent within the body beyond the time when assayable levels in the serum are demonstrable. The therapeutic results obtained indicate the feasibility of ambulatory treatment of syphilitic patients with penicillin in an oily vehicle.

ARCH. INT. MED., CHICAGO

- Gastroenterology. A review of the literature from July 1946 to July 1947. [Lymphogranuloma venereum.] Joseph B. Kirsner, Walter Lincoln Palmer, William E. Ricketts, Grayson F. Dashiell and Julian W. Buser. 81: 534–598, Apr. 1948; 746–790, May 1948.
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- *Jarisch-Herxheimer reaction in neurosyphilis treated with penicillin. Mark T. Hoekenga and Thomas W. Farmer. 82: 611–622, Dec. 1948.
- Syphilis. A review of the recent literature. Harold A. Tucker, Charles F. Mohr, Richard D. Hahn and Joseph Earle Moore. Progress in internal medicine. 83: 77–115, Jan. 1949; 197–246, Feb. 1949.

Jarisch-Herxheimer reaction in neurosyphilis treated with penicillin. Mark T. Hoekenga and Thomas W. Farmer. Arch. Int. Med., 82: 611–622, 1948.

This paper presents data concerning Herxheimer reactions based on a study of 349 neurosyphilis patients, at the Johns Hopkins Hospital, who were treated with aqueous penicillin between 1944 and 1948. Penicillin was administered intramuscularly in initial doses ranging from 30,000 to 300,000 Oxford units within the first 6 hours. Rectal temperatures were recorded every 2 to 4 hours. A rise in temperature above 100° F. (37.8° C.) was considered to be a febrile reaction. No comparison is made of Herxheimer reactions observed during penicillin therapy with those observed during other methods of treatment.

The total incidence of febrile reactions in the 349 patients with various types of neurosyphilis was found to be 34 percent. In the incidence of reactions demonstrated there was no relationship to race or sex differences, duration of infection with syphilis, serologic titer of the blood, or to the penicillin dosage (above a threshold level of 20 units per kilogram). The diagnostic type of neurosyphilis and the degree of abnormalities in the cerebrospinal fluid were found to definitely influence the incidence of reaction. Febrile reactions occurred in approximately 75 percent of the patients with dementia paralytica as compared with only 25 percent in patients with all other types of neurosyphilis. The incidence was higher in patients, particularly those with dementia paralytica, in whom the white blood cell count and total protein content were abnormal, and in those who had strongly positive reactions to complement-fixation tests of the cerebrospinal fluid. There was no significant difference in the incidence of reaction between patients who had received recent metal chemotherapy and those previously untreated. The patterns of fever in the patients were variable. Maximal responses occurred in 4 to 24 hours after the injection of penicillin, the greatest elevations in temperature occurring between 12 and 16 hours in approximately 50 percent of the patients.

After small initial doses of penicillin (20 units per kilogram), the incidence of febrile reactions was approximately the same as that seen after the usual therapeutic doses (2,500 to 5,000 units per kilogram). In neurosyphilis, febrile reactions cannot be avoided by administration of repeated small doses of penicillin.

In view of the above, the author states that there is need for additional study of the Herxheimer reaction in neurosyphilis patients, particularly those with dementia paralytica.

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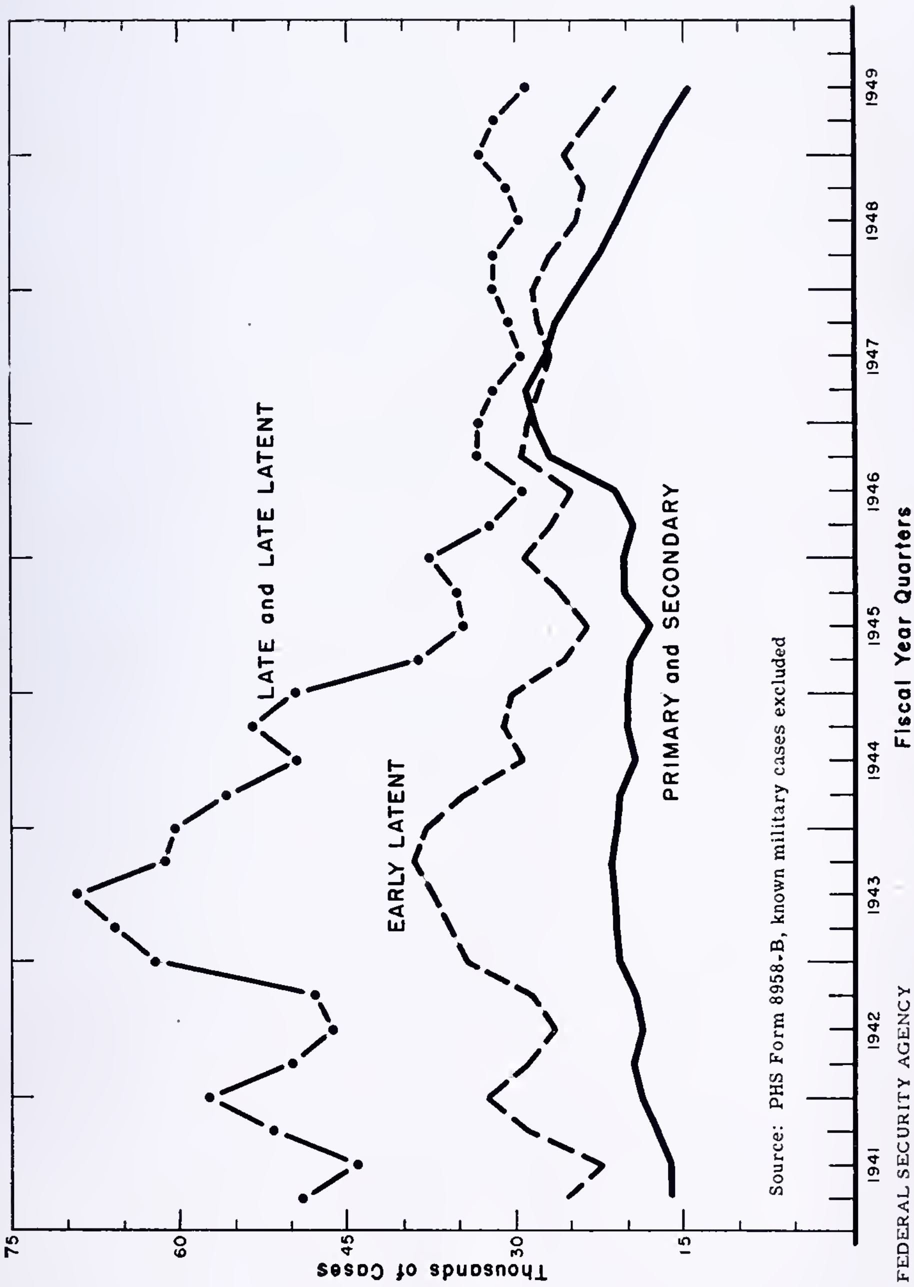
CASES OF ACQUIRED SYPHILIS REPORTED BY STATES AND TERRITORIES
FISCAL YEAR QUARTERS 1941 TO DATE



Source: PHS Form 8958-B, known military cases excluded

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The JOURNAL of VENEREAL DISEASE INFORMATION

Volume 30 August 1949 Number 8

ORIGINAL ARTICLES

Reports of the North Carolina Syphilis Studies. III. An Evaluation of Case-Finding Measures in the Control of Gonorrhea 211
John J. Wright, M. D., M. P. H.
Cecil G. Sheps, M. D., M. P. H.

The Role of Cardiolipin Antigens in the Serology of Syphilis 217
R. C. Arnold, *Senior Surgeon*
J. F. Mahoney, *Medical Director*

A Report of Spinal Fluid Findings in Patients Who "Relapsed" Following Penicillin Therapy for Early Syphilis 219
Andrew P. Sackett, *Surgeon*
Hunter Boggs, M. D.

CURRENT NOTES AND REPORTS 224

CURRENT LITERATURE 226

STATISTICS

Reported Civilian Venereal Disease Cases and Rates per 100,000, Fiscal 1948 239

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Reports of the North Carolina Syphilis Studies[1]

III. An Evaluation of Case-Finding Measures in the Control of Gonorrhea

John J. Wright, M. D., M. P. H., and Cecil G. Sheps, M. D., M. P. H.

Introduction

In previous communications (*1*, *2*), the authors have discussed the importance of careful evaluation of the effectiveness of case-finding measures in syphilis control. The organization and field of operation of the North Carolina Syphilis Studies have been described (*1*). Although these studies have been devoted to syphilis incidence and prevalence and its control program, it was possible, in addition, to arrange for careful records to be kept relating to certain aspects of the cases of gonorrhea which came to the attention of the health department. The purpose of this paper is to report on an analysis of the origin of 2,061 cases of gonorrhea in order to determine the relative effectiveness of the major case-finding procedures in gonorrhea control in an urban area served by a health department carrying on an average type of venereal disease control program. Also reported is an analysis of the results of the investigation of 1,015 consecutive contacts of gonorrhea.

Method of Study

The data presented in this communication include all the patients with gonorrhea diagnosed at the Durham City and County Health Department during the period January 1, 1946, through June 30, 1948, who were interviewed with a view to determining, among other things, the factor responsible for bringing each patient to diagnosis.

Criteria for diagnosis were based upon reliable positive findings in at least two of the following fields: Clinical and epidemiologic history, physical findings, and laboratory examinations, including cultures and fermentation tests.

A number of individuals were included more than once because they were diagnosed as having had one or more gonorrhea reinfections. In addition to clinical findings, the following criteria were used in making a diagnosis of gonorrhea reinfection:

1. Females—a period of at least 6 months since previous diagnosis or a shorter period, provided that there had been at least three negative cultures with menstrual periods intervening.

2. Males—no time consideration, clinical basis only.

An analysis of the results of the investigation of all the contacts of gonorrhea reported to the health department for the year 1947 is also included. This groups was comprised of contacts about whom information was obtained in the health department itself and also those who were reported from outside its jurisdiction.

Classification of Origin of Cases

The classification used is a functional one in terms of what brought the patient to recognition as a case of gonorrhea, regardless of the referral agency. The case-finding procedures which brought these cases to attention fall into three groups, each of which requires quite different activities on the part of the health department:

1. Epidemiology or contact investigation—administrative and field effort directed toward selected individuals.

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[1] From the School of Public Health, University of North Carolina.

These studies are supported jointly by grants from the International Health Division of the Rockefeller Foundation and the North Carolina State Board of Health.

Presented at the Eleventh Annual Session of the American Venereal Disease Association, Washington, D. C., April 8, 1949.

2. Voluntary application or the patient's initiative—possibly the result of educational effort directed at groups which may or may not be selected.

3. All other methods—routine, premarital, prenatal, food handlers, suspects, military, etc.

Classification of Results of Contact Investigation

There are two classes of contacts: those who were not located and those who were. The primary reasons for not locating contacts were insufficient or incorrect identifying information or that the contact had moved outside the jurisdiction of this health department. The contacts who were located were grouped as follows:

1. Gonorrhea present and brought to treatment.
2. Already under treatment for gonorrhea.
3. Negative for gonorrhea.
4. Failed to complete examination.

Results of Study

In the 30-month period ending June 30, 1948, 2,061 cases of gonorrhea diagnosed in the health department were analyzed. The number of cases of gonorrhea diagnosed during that time was greater than the number of cases interviewed because of lack of personnel. Table 1 shows the distribution of cases diagnosed and cases interviewed, by race and sex. It is seen that 69.2 percent of the patients were interviewed. Since, under the pressure of work, it was not possible to interview all, choices were made by the clinic staff on the following basis:

1. Included at all times: Sulfa-resistant cases prior to the administration of penicillin.
2. Omitted when necessary:
    (*a*) Patients deemed to be uncooperative.
    (*b*) Wives of known infected males.

Only one of these factors—wives of known infected males—creates a bias in favor of interviewing more male than female cases. This probably accounts for the fact that more of the male than of the female cases were interviewed in the health department studied.

Table 1.—*Cases of gonorrhea diagnosed and interviewed, by race and sex*

Race and sex	Cases of gonorrhea		Cases interviewed	
	Number	Percent	Number	Percent
Negro:				
Male	1,725	58	1.289	62.5
Female	914	30.7	546	26.5
White:				
Male	220	7.4	172	8.3
Female	117	3.9	54	2.6
Total	2,976	100	2.061	100

Analysis of Data

The data for the interviewed cases of gonorrhea were classified and tabulated by case-finding method, race, and sex. The data relating to the results of investigation of contacts of gonorrhea were classified and tabulated by disposition of case, race, and sex.

The tables present the data which are discussed. It will be noted that in some instances the percentages do not add up to precisely 100 percent. These differences in summation are due to rounding.

Origin of Cases by Race and Sex

Table 2 and figure 1 show the origin of all cases, by race and sex. From the point of view of race differences, attention is drawn to the fact that among the white cases a higher proportion came to diagnosis on their own initiative in

Table 2.—*Origin of cases of gonorrhea, by race and sex*

Origin of case	Negro				White				Total	
	Male		Female		Male		Female			
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Contact investigation	78	6	399	73	2	1.2	32	59.2	511	24.8
Patient's initiative	1,177	91.3	76	13.9	169	98.2	16	29.6	1,438	69.8
Other	34	2.6	71	13.0	1	.6	6	11.1	112	5.4
Total	1,289	100	546	100	172	100	54	100	2,061	100

both sexes than in the Negro cases, the proportions being 98.2 percent of the white males against 91.3 percent of the Negro males; and 29.6 percent of the white females against 13.9 percent of the Negro females.

A striking difference is obvious in the relative effectiveness of the major case-finding procedures between the sexes in both races, even though some wives of infected males were omitted from the study. In Negro males, contact investigation was responsible for the discovery of only 6 percent of the cases and the patient's initiative for 91.3 percent, whereas in Negro females the respective

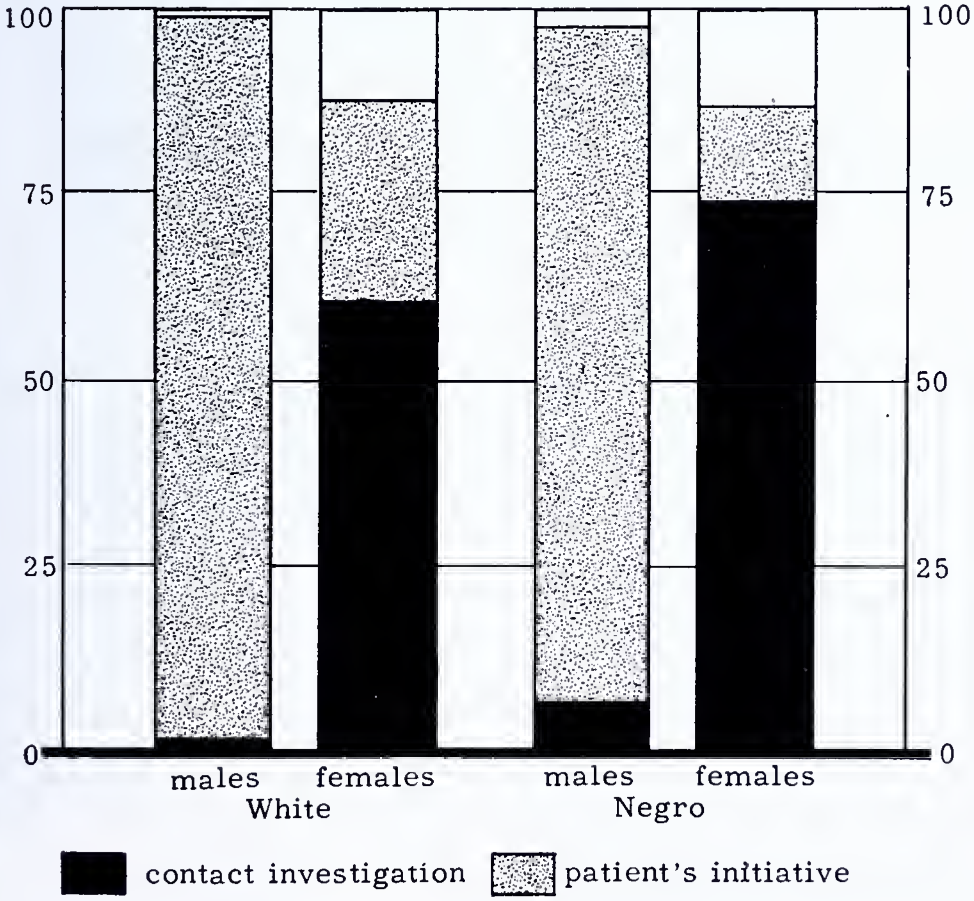

Figure 1.—Origin of cases, by race and sex.

proportions were 73 percent and 13.9 percent. In white males, contact investigation was responsible for discovering 1.2 percent of the cases and the patient's initiative for 98.2 percent, whereas in white females the respective proportions were 59.2 percent and 29.6 percent.

The distribution of case-finding procedures as described in this section was found to be highly significant statistically.[2]

Results of Contact Investigation, by Race and Sex

Table 3 and figure 2 show the results of investigation of gonorrhea contacts by race and sex. The data analyzed include only those cases which were located. An additional 204 contacts reported during the year were not located. Thus, the group analyzed represents 83.3 percent of the gonorrhea cases reported to this health department in 1947.

Table 3.—*Results of investigation of gonorrhea contacts, by race and sex*

Result of investigation	Negro				White				Total	
	Male		Female		Male		Female			
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Brought to treatment	51	13.1	329	58.2	0	0	23	63.9	403	39.7
Already under treatment	194	49.9	123	21.8	13	52.0	6	16.7	336	33.1
Not infected	134	34.4	106	18.8	11	44.0	6	16.7	257	25.3
Incomplete examination	10	2.6	7	1.2	1	4.0	1	2.7	19	1.9
Total	389	100	565	100	25	100	36	100	1,015	100

In tabulating the disposition of the contacts who were reported more than once during the same period and who were brought to treatment by the investigation, such patients were counted once as being "brought to treatment" and subsequently as "already under treatment." This analysis as to results of investigation refers to gonorrhea only and does not take into account other venereal disease, since the aim was to assess the value of the investigation of gonorrhea contacts as a gonorrhea case-finding measure.

The data demonstrate a marked sex difference in the proportion of contacts brought to treatment as a result of the investigation. This is true in both races. The proportion of Negro male contacts brought to treatment was 13.1 percent as compared with 58.2 percent for Negro females. This sex difference was very significant statistically. The comparable proportions for the white contacts, though much smaller in number, are similar in their distribution.

Another striking and statistically significant sex difference is seen in the proportion of contacts in both races found on investigation to be already under treatment for gonorrhea. The proportion of Negro male contacts already under treatment was 49.9 percent as compared with 21.8 percent for Negro females. For the white contacts, the comparable proportions were: males, 52.0 percent, and females, 16.7 percent.

In both races a statistically significant sex difference was observed between the proportion of contacts found to be free of gonorrheal infection. The proportion of Negro male contacts who were not infected was 34.4 percent as compared with 18.8 percent for Negro females. The comparable proportions for the white contacts were males, 44.0 percent, and females, 16.7 percent.

Discussion

The effectiveness of penicillin in the treatment of gonorrhea has simplified the

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[2] Grateful acknowledgment is made to the Institute of Statistics, Greater University of North Carolina, for assistance with this phase of the analysis.

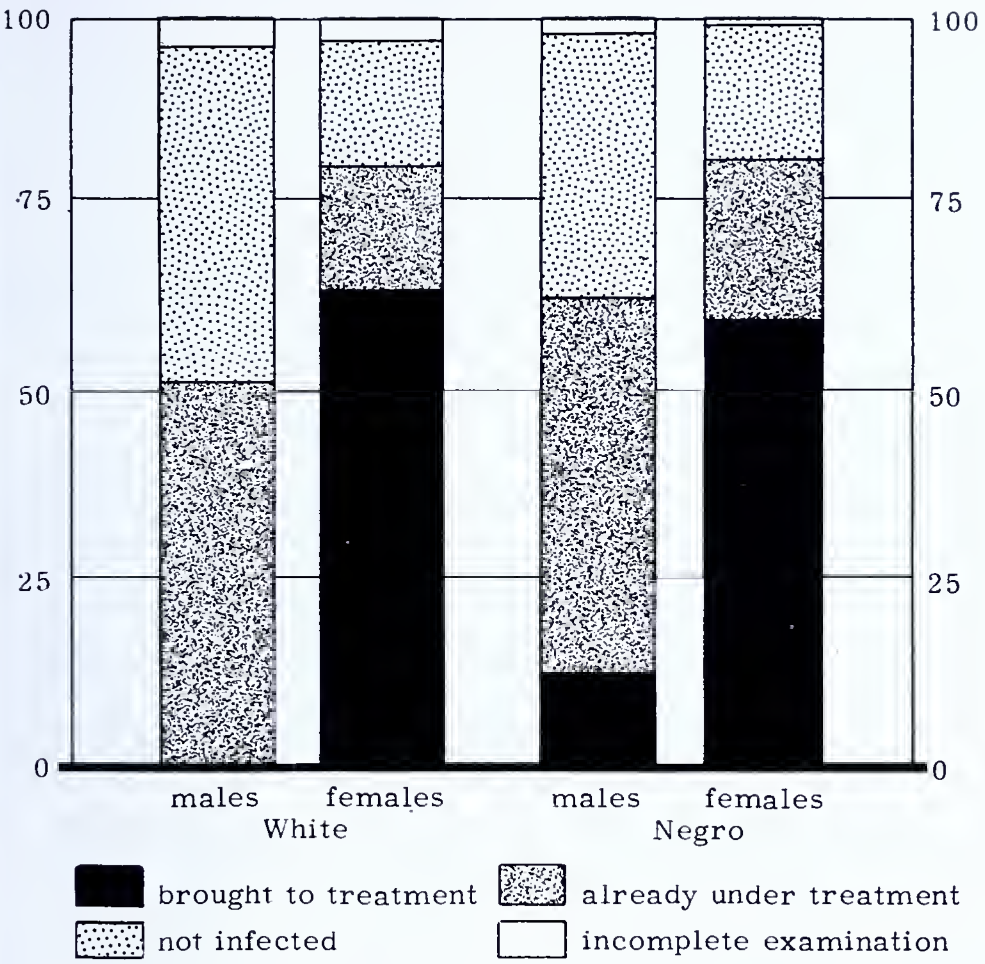

FIGURE 2.—Results of investigation of gonorrhea contacts, by race and sex.

problem of gonorrhea control by reducing the importance of case holding. This development, however, serves to emphasize the importance of case finding. Careful studies are therefore needed to evaluate the relative effectiveness of the major case-finding technics in gonorrhea control in order to provide a basis for finding the administrative compromise which is necessary between effectiveness and economy. This is of particular importance with reference to the evaluation of contact investigation, because it may be expected that an increasing proportion of gonorrhea cases will be treated by private practitioners. If serious attempts are to be made to develop the use of this epidemiologic approach with private patients, it behooves us to be reasonably certain of the value of such a program.

The literature which sheds some light on this matter is largely confined to analysis of health department data with a view to determining how many new cases of gonorrhea are found per original patient (*3*) or per contact named (*4*). It is probable that studies of that type form the basis of the statement made by Gillis (*5*) in 1948, "The experience gained during the war proved that investigation of gonorrhea contacts is one of the most difficult, expensive, and variable phases of venereal disease control." While this statement may on the whole be true, it would appear from our analysis that there are certain segments of this problem in which contact investigation plays a more reliable and vital role than in others.

When the data relating to the origin of cases of gonorrhea are broken down on a race-sex-specific basis, reliable and useful information is obtained. In this connection it is pointed out that, in this health department, equal effort was exerted in the follow-up of both male and female contacts. In actual practice the investigators, before proceeding on their daily rounds, would sort out their contact slips on the basis of geographic proximity without regard to the sex of the contact. There is a striking difference in the effectiveness of contact investigation between the sexes. It is responsible for bringing to recognition 73 percent of the Negro females and 59.2 percent of the white females. The role of contact investigation in males was much less important, providing only 6 percent of Negro cases and 1.2 percent of white cases.

Our data indicate that the patient's initiative is somewhat more reliable as a case-finding measure among whites than among Negroes. This was responsible for bringing to diagnosis 98.2 percent of the white males as against 91.3 percent of Negro males, and for 29.6 percent of white females as compared with 13.9 percent of Negro females.

These data indicate quite clearly that if this health department had relaxed its efforts in contact investigation, more than half of the female cases of gonorrhea would have come to attention and control later than they did, if at all. This suggests that educational effort aimed at raising the "level of suspicion" of the lay person as to the possibility of urogenital symptoms being due to gonorrhea was either not reaching females to the same degree as males, or that females have a greater tendency to ascribe such disturbances to causes other than veneal disease.

The analysis of data relating to the results of contact investigation indicates that there is a striking difference, on a sex-specific basis, in the effectiveness of this procedure as a case-finding measure in the control of gonorrhea. This is of some importance from the administrative point of view. Among the Negro contacts, for example, more females were infected (80 percent) than were the males (63 percent). Furthermore, of the infected females, almost three-quarters (72.8 percent) were not under treatment when investigated, whereas, of the infected males, less than one-quarter (20.8 percent) were not under treatment when investigated. Expressed somewhat differently, it might be said that these data indicate that for every 100 female contacts located, 58.2 cases of gonorrhea were brought under control, whereas, for every 100 male contacts located, only 13.1 cases were brought under control—a ratio of somewhat more than 4 to 1. The comparable proportions for the white contacts are similar, although the numbers involved are much smaller.

Conclusions

1. Accurate information regarding the relative effectiveness of the major case-finding measures in the discovery of new cases is essential for the development and maintenance of an adequate gonorrhea control program. This knowledge is obtained from a careful analysis of the data relating to the origin of such cases, with special attention being paid to sex differences. The analysis of 2,061 cases of gonorrhea diagnosed in an urban health department in the southern United States indicates that:

(*a*) Contact investigation was responsible for bringing to diagnosis the greatest proportion of female cases.

(*b*) The patient's initiative was responsible for bringing to diagnosis the greatest proportion of male cases.

(*c*) Educational effort, as evidenced by the proportion of cases coming to attention on the patient's initiative in the period studied, was more effective among whites than among Negroes.

2. Valuable information on the effectiveness of contact investigation as a case-finding measure in the discovery of untreated cases of gonorrhea can be obtained by analyzing the results of such activity on a sex-specific basis. This analysis of the disposition of 1,015 gonorrhea contacts who were located indicates that:

(*a*) A greater proportion of female than of male contacts were found to be infected.

(*b*) Of those who were infected, a much greater proportion of the males than of the females were found to be already under treatment.

(*c*) The number of previously untreated cases of gonorrhea brought under control as a result of the investigation of 100 female contacts was more than four times the number of such cases resulting from the investigation of 100 male contacts.

Acknowledgment

The authors wish to express appreciation to the Superintendent of the Durham City and County Health Department and to the Director and staff of its Venereal Disease Clinic, whose cooperation made this study possible.

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The Role of Cardiolipin Antigens in the Serology of Syphilis[1]

R. C. Arnold, Senior Surgeon, and J. F. Mahoney, Medical Director,[2] United States Public Health Service

Cardiolipin as a new antigenic component has now assumed a major role in the serology of syphilis. In less than a decade the word "cardiolipin" has become almost a generic term meaning—a pure antigenic substance, a pure chemical, an antigen, a test, a type of test, or a diagnostic criterion. The isolation and purification of cardiolipin by Pangborn gave impetus to the development of new antigens, new testing procedures, and the modification of existing technics for cardiolipin-type antigens. The syphilologists and serologists have observed the desirable qualities related to sensitivity and specificity of the new-type antigen. In the remodeled serologic structure, however, the multiplicity of lipoidal and cardiolipin tests and the noticeable discrepancy of serologic reports in the diagnostic or qualitative range have created unfavorable and even confusing impressions. At times, undue significance may have been placed on the value of incomplete reactions in the weakly positive or doubtful zone. It is time to delineate the role of cardiolipin in the serology of syphilis and nonspecific diseases.

Cardiolipin is a purified chemical extract of beef heart which, when properly combined with lecithin and cholesterol, forms a serologic antigen. Cardiolipin is not completely new; it is present in varying proportion in all beef heart lipoidal extracts and may influence their sensitivity and specificity as antigenic substances.

The isolation and purification of cardiolipin from beef heart is a comparatively prolonged and difficult process of chemical extraction. The finished product must pass rigid standards of purity before it may be used. Equally important in the composite antigen is the lecithin component, which must be prepared with the same care and must meet equally rigid standards of purity. The third component of the antigen, chemically purified cholesterols, appears to be satisfactory. A complete antigen is compounded by adding the proper proportions of the three components to ethyl alcohol. In addition to the chemical standardization, a serologic assay must be conducted to determine the relationship of the antigenic properties.

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[1] Presented at the symposium on "Current Progress in the Study of the Venereal Diseases, 1949."

[2] Venereal Disease Research Laboratory, U. S. Marine Hospital, Staten Island 4, N. Y.

A properly prepared cardiolipin antigen is believed to be more specific than the older lipoidal antigens. Moreover, its sensitivity may be adjusted and maintained at a determined level. This level should be established by clinical and serologic studies, so that serologic reports will give the clinician the necessary information in treated and untreated syphilis but will minimize the number of biologic false-positive reactions. The selection of an optimal level of sensitivity for a standard cardiolipin antigen will not be easy because of the many factors involved.

A positive result may be obtained in serum from patients who have untreated syphilis, relapsing syphilis, adequately treated syphilis, and certain diseases, such as malaria, infectious mononucleosis, and others that cause biologic false-positive reactions. Since a positive test does not indicate the active presence of *Treponema pallidum*, the interpretation and evaluation of the positive report must be made by the physician. The positive reaction indicates only that a reactive substance (reagin) of some type is present in the serum. The quantity of reactive substance varies with each individual in health and in disease. A level of sensitivity could be established which would produce a great many or relatively few positive reports, but the extremes would not be suitable for either diagnostic or posttherapeutic studies. A certain level of sensitivity (which may be higher or lower than the present concept) may produce sufficient information in terms of syphilis and yet be relatively free from biologic false-positive reactions.

In considering an antigen for public health use, one must realize that it may be employed in widely separated geographic and climatic areas of this country or even throughout this hemisphere. Hence, it may be necessary to study several different antigen sensitivity levels on serum from both healthy and diseased individuals in order to secure the necessary data for determining the optimal level of sensitivity. Already one combined clinical and laboratory study is being formulated to survey this problem in untreated and treated syphilis.

Another source of confusion in the serology of syphilis is the discrepancy which occurs when several test procedures are reported. Many tests in common use today employ not only a cruder lipoidal antigen but also an antigen containing cardiolipin and purified lecithin. The results produced by these two antigens, even in the same test, are not always in agreement. Nor do two different tests utilizing cardiolipin-lecithin antigens always react similarly. It is little wonder that the patient, and sometimes the physician, may be bewildered. The obvious solution to this problem is the use of recognized standard procedures.

Under the authority of the Coordinating Committee on Laboratory Methods of the American Public Health Association, a committee has been formed for the purpose of formulating, evaluating, and establishing reference-standard serologic methods for the serodiagnosis of syphilis. Having once been established, these reference-standard tests could become part of the *Diagnostic Procedures and Reagents* of the American Public Health Association and could function as do standard methods in the fields of milk and water analysis. The development and adoption of the standard antigens and tests for syphilis by the State laboratories would not preclude the use of diagnostic procedures that are now employed and may be preferred in the hospital, clinic, or private laboratories.

Since the advent of rapidly completed and adequate antisyphilitic therapies (first, intensive arsenotherapy and now, penicillin), more patients with early syphilis are becoming seronegative; also, fewer patients are remaining in the seropositive latent classification, and fewer late manifestations are being observed. With the shrinkage of the reservoir of syphilitic patients, the biologic false-positive potential becomes more important. The number of individuals with biologic false-positive reactions actually may be increasing, or the increase may be only a relative one in relation to syphilitic patients. With further extension of adequate penicillin therapy, one may expect the ratio to change even more in the coming decades.

It is, therefore, increasingly important that only tests of adequate specificity be retained. The increase of specifiicity-potential contributed by cardiolipin-lecithin antigen to tests for syphilis seems to indicate that this type of antigen is to be recommended until more specific reagents are evolved.

A Report of Spinal Fluid Findings in Patients Who "Relapsed" Following Penicillin Therapy for Early Syphilis[1]

Andrew P. Sackett, Surgeon,[2] United States Public Health Service, and Hunter Boggs, M. D.[3]

In the course which syphilis runs, by far the greatest amount of disability and mortality arises from the late manifestations of the disease. One of the most dreaded of these developments is neurosyphilis in its various clinical forms. The question which arises regarding the ability of penicillin therapy as administered for early syphilis to prevent the development of neurosyphilis is an important one. Certainly enough time has not elapsed for a final answer to be made to this question. However, a study of spinal fluid findings in a group of patients having early syphilis who failed following penicillin therapy might give some clue as to what may be expected in this regard.

This paper is a study of 437 patients with early syphilis who relapsed following penicillin therapy. The schedules of treatment which were used on original admission are as follows:

1. The 2.4 schedule: 2,400,000 units penicillin (40,000 every 3 hours for 8 days).
2. The fever-penicillin schedule: 600,000 units penicillin plus 10 hours of fever over 104° F. in one session (20,000 units every 3 hours for 5 doses before fever, 80,000 units every 3 hours for 5 doses on day of fever session, and 20,000 units every 3 hours for 5 doses after fever session).
3. The 8-6-3 schedule: 600,000 units penicillin (10,000 every 3 hours for 8 days), with 1 mg. of arsenoxide per kilogram of body weight to a maximum of 60 mg. for 8 days, and 200 mg. of bismuth on the 1-5-8th days.
4. The 5-12-3 schedule: 1,200,000 units penicillin (10,000 every 3 hours for 15 days), with 1 mg. of arsenoxide per kilogram of body weight to a maximum of 60 mg. on the 1-3-5-7-9th days, and 200 mg. of bismuth on the 1-5-9th days.
5. The 5-12-0 schedule: 1,200,000 units penicillin (10,000 every 3 hours, for 15 days), with 1 mg. of arsenoxide per kilogram of body weight to a maximum of 60 mg. on the 1-3-5-7-9th days.

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[1] From the Kanawha Valley Medical Center, South Charleston, W. Va.

[2] Formerly Medical Officer in Charge.

[3] Consultant in Dermatology and Syphilology.

6. The 5-28-3 schedule: 2,800,000 units penicillin (25,000 every 3 hours for 14 days), with 1 mg. of arsenoxide per kilogram of body weight up to a maximum of 60 mg. on the 1-4-7-10-13th days, and 200 mg. of bismuth on the 1-7-13th days.

7. The 5-18-3 schedule: 1,800,000 units penicillin (16,667 every 2 hours for 9 days), with 1 mg. of arsenoxide per kilogram of body weight up to a maximum of 60 mg. on the 1-3-5-7-9th days, and 200 mg. of bismuth on the 1-5-9th days.

The number of patients treated with each of the schedules was as follows:

Treatment schedule	*Number of patients with early syphilis*
2.4	6
Fever-penicillin	24
8-6-3	86
5-12-3	79
5-12-0	62
5-28-3	47
5-18-3	133
Total	437

Spinal fluid findings in this group at the time of re-treatment are compared with the findings in the same group of individuals at the time of original treatment. This group includes 349 patients with primary and secondary syphilis and 88 patients with early latent syphilis. It does not include 26 patients who, after careful evaluation of available data, were classed as probable reinfections. To differentiate between relapse and reinfection is almost always difficult and many times is impossible. However, that consideration does not invalidate the data, since this is not a comparison of the two conditions but rather a report of findings in patients who, insofar as we could determine, had suffered a relapse. Patients on whom spinal fluid examinations were not done on both first admission and on readmission are not included. Similarly, patients who were re-treated because the spouse had a relapse but who had no clinical or serologic evidence of relapse themselves are not included.

Data presented in table 1 indicate the percentage of patients in each of the diagnostic categories who had abnormal spinal fluid findings. Of the total group, the spinal fluid examinations of 12.9 percent were abnormal. This corresponds closely with the 13.9 percent abnormal spinal fluids among 567 patients with primary and secondary syphilis reported by Dattner (*1*) and indicates that the group herein studied is not characterized by a higher incidence of abnormal spinal fluid findings than one might expect to find in any group of primary and secondary syphilis cases. Conversely, this would tend to indicate that abnormal spinal fluid findings in primary and secondary syphilis do not predispose to relapse.

In classifying the spinal fluids with respect to degree of abnormality, the classifications used were Moore's group 1, group 2, and group 3 (*2*). For purposes of grouping the spinal fluids, we considered a count of eight or more white blood cells per cubic millimeter of fluid to be abnormal and a total protein determination of more than 40 mg. percent to be above the limits of normal. Of the 45 who had abnormal fluids at the time of first admission, 36 were group 1, 8 were group 2, and 1 was of group 3 intensity. Of the 36 which were group 1 on first admission, 14 were negative on

Table 1.—*Spinal fluid findings on first admission*

Diagnosis on first admission	Number of patients	Group 1	Group 2	Group 3	Total number abnormal	Percent abnormal
Seronegative primary	23	2	0	0	2	8.7
Seropositive primary	64	5	0	1	6	9.4
Secondary	253	25	7	0	32	12.7
Secondary relapse [1]	9	4	1	0	5	55.6
Total	349	36	8	1	45	12.9

[1] 7 of these followed inadequate heavy metal therapy elsewhere and 2 were subsequent to penicillin therapy elsewhere. The latter 2 had normal spinal fluid findings.

readmission, 20 were still group 1, and 2 had progressed to group 2. Of the 8 with group 2 findings on first admission, 3 were negative on readmission, 2 were group 1, and the remaining 3 were still group 2. The one patient who had group 3 findings on first admission was group 1 on readmission. Of the entire group of 45, 17 were negative on readmission, and 3 which were still positive on readmission were less strongly positive. Thus 20 (44.4 percent) were actually improved on readmission as far as spinal fluid findings are concerned, 23 (51.1 percent) were of the same group, and only 2 (4.4 percent) had progressed in the sense of having become more strongly positive. There is, therefore, no tendency for patients with abnormal spinal fluids to develop progressively more severe spinal fluid abnormalities upon relapsing after penicillin therapy. This is in striking contrast to the data of the Cooperative Clinical Group (*3*), which showed that, of patients whose blood test relapsed from negative to positive following routine treatment for early syphilis, 28.8 percent had a similar relapse of the spinal fluid test to positive, and that, of patients whose spinal fluid type had previously been group 1 or group 2, with the relapse of the blood test, the spinal fluid became more positive in 50 percent of the early cases.

Table 2 gives a detailed break-down of this material. Of the patients who had abnormal spinal fluids on first admission, 62.2 percent had abnormal spinal fluid findings at the time of re-treatment. Of the patients who had normal spinal fluid findings on first admission, 14.5 percent had abnormal spinal fluid findings at the time of re-treatment. Thus, the primary or secondary syphilis patient who had abnormal spinal fluid findings when first treated had four to five times as many abnormal spinal fluid findings when and if he relapsed than the patient who had normal spinal fluid when first examined. Of the 349 patients who had primary or secondary syphilis on first admission, 20.6 percent had abnormal spinal fluid findings on readmission. When compared with the 12.9 percent of the same group who had abnormal spinal fluids on first admission this is seen to represent an increase of 7.7 percent, an increment of approximately one-half. In addition to this, of the 88 patients whose diagnosis on first admission was early latent syphilis, 5 or 5.7 percent had abnormal spinal fluid findings on readmission.

Group 2 and group 3 findings have a much graver prognostic import than

Table 2.—*Status of spinal fluid on readmission of relapsed patients with early syphilis*

Diagnosis and status of spinal fluid on first admission	Number of patients	Status of spinal fluid on readmission					Percent abnormal on readmission
		Normal	Abnormal				
			Group 1	Group 2	Group 3	Total	
Total patients	437	360	57	17	3	77	17.6
Early latent	88	83	4	1	0	5	5.7
Primary and secondary	349	277	53	16	3	72	20.6
With abnormal spinal fluid	45	17	23	5	0	28	62.2
Seronegative primary	2	1	1	0	0	1	50.0
Seropositive primary	6	2	4	0	0	4	66.7
Secondary	32	13	14	5	0	19	59.4
Secondary relapse	5	1	4	0	0	4	80.0
With normal spinal fluid	304	260	30	11	3	44	14.5
Seronegative primary	21	17	3	1	0	4	19.1
Seropositive primary	58	53	3	0	2	5	8.6
Secondary	221	186	24	10	1	35	15.8
Secondary relapse	4	4	0	0	0	0	0.0

group 1 findings (*4*). If group 2 and group 3 fluids are considered, we find that in this group of 437 patients, there were only 9 whose spinal fluid findings were so classed when first admitted. When examined on readmission, there were 20 patients who had fluids with abnormal findings of group 2 or group 3 intensity.

According to Moore (*5*), the incidence of early meningeal neurosyphilis is increased at least tenfold by the inadequate heavy-metal treatment of early syphilis. In this series of penicillin-treated cases, consisting exclusively of treatment failures, the incidence of abnormal fluids is less than double the original incidence. If this finding is of any prognostic import, the incidence of meningeal neurosyphilis in the entire pencillin-treated group will be much lower than that following the irregular type of routine conventional treatment which was formerly the rule in most public clinics. In this series of 437 patients, there was only one symptomatic neurorecurrence, a case of acute syphilitic meningitis which developed approximately 11 months after the 5-18-3 schedule of treatment for seropositive primary syphilis.

Table 3 shows a break-down by the type of relapse encountered by each group of patients. Of the total group, 60.9 percent of the relapses were mucocutaneous and 39.1 percent were serologic. This is a higher percentage of mucocutaneous relapses than occurs in patients who relapse following routine treatment, since, according to Stokes (*6*), the two occur in such patients with approximately the same frequency. This increase in numbers of mucocutaneous relapses in comparison with the number of serologic relapses might be anticipated due to the more rapid completion of treatment, the patient thus having an opportunity to relapse closer to the time the infection was acquired. This is of some importance, because the patient who suffers a mucocutaneous relapse is more likely to be aware of his condition, even though he has not been getting serologic follow-up, and consequently to return for reexamination, whereas the patient who suffers a serologic relapse and who also does not obtain serologic follow-up is not similarly warned. It is also of some public health significance, because patients with mucocutaneous relapses are more infectious than those having a serologic relapse.

Of the 248 patients whose original diagnosis was primary or secondary syphilis and who suffered a clinical relapse, 43 (17.3 percent) had abnormal spinal fluid findings. Of the 101 patients whose original diagnosis was primary or secondary syphilis and who suffered a serologic relapse, 29 (28.7 percent) had abnormal spinal fluid findings on readmission. This difference in incidence of abnormal spinal fluid findings in mucocutaneous and serologic relapses is possibly great enough to be significant and if so would indicate that, if none of this group were given further treatment, those suffering serologic relapses would eventually demonstrate a higher incidence of symptomatic neurosyphilis. If this is true it is unfortunate, because the tendency of these patients to fail to return for re-

Table 3.—*Break-down by original diagnosis, type of relapse suffered, and the spinal fluid findings on readmission*

Diagnosis on first admission	Total number of relapses	Mucocutaneous relapses		Serologic relapses	
		Normal CSF on readmission	Abnormal CSF on readmission	Normal CSF on readmission	Abnormal CSF on readmission
Seronegative primary	23	18	4	0	1
Seropositive primary	64	49	6	6	3
Secondary	253	134	22	65	22
Secondary relapse	9	4	1	1	3
Early latent	88	18	0	65	5
Total	437	223	43	137	34

treatment is probably greater than in the group suffering mucocutaneous relapses.

Summary

1. The incidence of abnormal spinal fluid findings in this group of 349 patients having primary and secondary syphilis who relapsed was 12.9 percent prior to treatment on first admission. This is no greater than the incidence of abnormal findings in the general run of patients having primary and secondary syphilis and therefore would indicate that abnormal spinal fluid findings in patients having primary and secondary syphilis do not predispose to relapse.

2. Of the 45 patients having primary and secondary syphilis with abnormal spinal fluid findings on first admission, 28 (62.2 percent) were abnormal on readmission. In only 2 patients (4.4 percent) had the spinal fluid findings become more strongly positive in the sense of having advanced to a more strongly positive group when classified on readmission. Thus, there is no tendency for patients with abnormal spinal fluids to develop progressively more severe spinal fluid abnormalities upon relapsing after penicillin therapy. This is in contrast to the situation following routine conventional treatment of patients having early syphilis with abnormal fluids; of such patients who relapsed, 50 percent became more positive (*3*).

3. One case of symptomatic neurorecurrence occurred in this series.

4. In this series of treatment failures, 60.9 percent were mucocutaneous relapses and 39.1 percent were serologic relapses. The incidence of spinal fluid abnormalities in those suffering serologic relapses was 28.7 percent, compared with 17.3 percent of those suffering a mucocutaneous relapse. The patient who suffers a serologic relapse is probably less likely to obtain further treatment than the patient who suffers a mucocutaneous relapse. Therefore, the higher incidence of spinal fluid abnormalities in the group suffering serologic relapses is unfortunate.

5. Of the 88 patients whose diagnosis on first admission was early latent syphilis, 18 (20.5 percent) suffered a mucocutaneous relapse and 79.6 percent suffered a serologic relapse. Only 5 (5.7 percent) had abnormal spinal fluid findings on readmission.

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Color Slides Illustrating the Lesions of Syphilis

Sets of 100 authentic color photographs of syphilitic lesions, placed on 2″ x 2″ glass mounts, are now available to private physicians, medical schools and centers, nursing and public health schools, and other interested groups.

These slides represent the best photographs contributed by the venereal disease and research centers throughout the United States. The Army, the Navy, State and local health departments, and several medical schools cooperated with the United States Public Health Service in making this collection possible. Final selection was made by the Division of Venereal Disease.

The following topics are covered:

1. Early acquired syphilis: primary and secondary.
2. Late syphilis: skin, bone and cartilage, and joints.
3. Congenital syphilis: early and late.

Each slide is appropriately captioned and fitted in a plastic leatherette case, 2½″ x 6″ x 10″ (weight 3½ lbs.). Any standard 2″ x 2″ projector can be used in showing these slides. A complete set, including case, may be purchased for $75 from the Creative Arts Studio, 1223 Connecticut Ave. NW, Washington 6, D. C.

"Facts on American Sports and Health"

A new popular-appeal approach in health education directed particularly at the teen-age group is being tried out in the booklet, "Facts on American Sports and Health," baseball edition. This eight-page publication, illustrated with drawings and cartoons in red and blue contains the 1949 major league schedules and their 1948 batting averages and pitching records, as well as believe-it-or-not bits on baseball's great. Interspersed among the baseball facts is information on syphilis, gonorrhea, cancer, tuberculosis, dental hygiene, and other health subjects. Although the booklet is written in a style to attract young people, it is considered appropriate for all age levels.

"Facts on American Sports and Health" is suitable for distribution at ball games, schools, playgrounds, etc. Priced at $50 per 1,000, this 8″ x 11″ program-style booklet may be obtained from the Communications Materials Center, Columbia University Press, New York 27, N. Y.

Newspaper Advertisements for VD Education

The Health Publications Institute in Raleigh, N. C., has a new publication containing advertisements for daily and weekly newspapers. This 10-page booklet, complete with facsimile advertising order blanks, contains 14 advertisements, each complete in itself. Each has a space for inserting a sponsorship line or the address and operating hours of the local clinic. Sponsorship may be by State, county, or municipal health departments or by a business or manufacturing establishment.

The advertisements give information about venereal diseases in simple, direct language, written in the form of patent medicine advertisements. Eight of the ads present facts about gonorrhea, six of them about syphilis. They are varied in approach and text so as to appeal to different reader interests and are best suited for continuous daily insertion in newspapers. Each ad is 1 column wide and approximately 50 lines long.

Voluntary health and welfare organizations and any other groups or individuals interested in obtaining this publication should write to the Division of Venereal Disease, United States Public Health Service, Washington 25, D. C., for sample copies. Mats of the 14 advertisements accompany the booklet. Additional mats will be supplied at cost by the Health Publications Institute, 216 North Dawson Street, Raleigh, N. C.

"Feeling All Right"—Newest VD Film

A documentary film, "Feeling All Right," has been produced for the State of Mississippi by the Southern Educational Film Production Service of the University of Georgia. Four southern States (Mississippi, Alabama, Arkansas, and Georgia) participated in planning it. The United States Public Health Service gave technical and financial assistance, but full sponsorship and supervision of production rested with the Mississippi State Board of Health.

The film was produced to meet the general need for a film which would set forth the facts about syphilis simply and forcefully enough to gain the confidence and cooperation of people not reached by other methods.

Released for preview in Mississippi in January 1949, by mid-April the film had been seen by over 100,000 Negroes in their churches, schools, and health departments. Within the next few months in Mississippi, a half million or more Negroes will see this film and receive VD comic books free of charge. Other States have already made arrangements to use the film in programs similar to that proving so successful in Mississippi.

"Feeling All Right" tells the story of Roy Jackson, a Negro youth who contracts syphilis. At first he takes the patent medicine recommended by his friend Jim. Jim and his wife, Ruby, had formerly been "cured" of their "haircut" by using the tonic. After attending a health lecture where symptoms of syphilis are discussed, Roy's mother persuades him to go to the health department for a blood test. Roy learns that he has syphilis and goes to the rapid treatment center to be cured. While there, he realizes the danger to Ruby's unborn child, but he gets home too late to prevent tragedy, for her baby has already died as a result of syphilis. Determined to avoid such a happening in his own family, Roy takes his girl, Irma, to her family doctor for a blood test. The film ends sometime after their marriage, with Roy and Irma introducing their healthy first-born child.

"Feeling All Right" also goes rather extensively into the symptoms, stages, and crippling results of syphilis. In spite of the large amount of instructional material in this film, it is free from stilted attitudes and has high entertainment value. None of the group were professional actors, but the photography, direction, and acting are excellent. While the general locale of the film is the cotton country between the Yazoo and the Mississippi Rivers, all scenes, characters, and accents were selected so as to seem familiar to people in nearly any section of the South. The message of "Feeling All Right" is one which is believed to have wide appeal to both white and Negro audiences.

Distribution of "Feeling All Right" will be handled solely by the Radio Bureau, School of General Studies, Columbia University, Broadway and 116th Street, New York, N. Y. The film, which is available in both 16 mm. and 35 mm., had a running time of approximately 30 minutes.

Medical Reference Material Needed for Chile

The newer reference materials in the medical school library of the University of Chile, including periodicals and books, were totally destroyed in the recent fire. Medical periodicals of the last 10 years and recent medical books are urgently needed, as well as any duplicate copies of the Index Medicus for the years 1879 through 1926. Any contributions will be appreciated and should be sent to the National Committee for Chile, room 318, Library of Congress, Washington 25, D. C.

Midwest Venereal Disease Control Seminar

A digest has been compiled of proceedings of the Midwest Venereal Disease Control Seminar held on February 17 and 18, 1949, in St. Louis, Mo.

Discussions at the seminar covered various topics, including the following:

1. Control measures: Venereal disease information at State and county fairs and in cities; contact investigation; implementation of military-civilian venereal disease control; contributions of the public health nurse and the schools of public health.
2. Treatment: Use of aureomycin and penicillin, especially procaine penicillin in oil with aluminum monostearate; various injection schedules.
3. Research: Experimental work in the cultivation of the *Treponema pallidum;* recent analytic work on penicillin in aluminum monostearate.

Mimeographed copies of this digest are available in small quantities without charge from the Regional Medical Director, United States Public Health Service, 69 West Washington St., Chicago 2, Ill.

CURRENT LITERATURE

NOTE: Abstracts of any article listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

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Impressions received during a study-trip to England and Scotland 1946. [V. D.] B. Tarras-Wahlberg. Transactions of the Swedish Dermatological Society for the Year 1946. 29: 296–301, Fasc. 3, 1949.

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Some experiences in the treatment of gonorrhea with aqueous solution of penicillin with glycerine in dispensary practice. Yrjö V. Salminen. 29: 388–396, Fasc. 4, 1949.

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Cardiovascular syphilis in young white males. John B. Schwedel and Kona Simon. Abstracts, Third Inter-American Cardiological Congress. 37: 675, Apr. 1949.

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Electro-narcosis: results in 125 patients with psychosis or psychoneurosis. [Syphilis.] Douglas Goldman. 217: 405–409, Apr. 1949.

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Carcinoma of the vulva. A review of fifty cases. [V. D.] Arthur B. Lunin. 57: 742–747, Apr. 1949.

Management of chronic endocervicitis in infertility. [Gonorrhea.] Leon Krohn, Joseph M. Harris, Maurice S. Priver, and Milton S. Fenmore. 57: 774–778, Apr. 1949.

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Studies of the combined action of antibiotics and sulfonamides. C. W. Price, W. A. Randall, Henry Welch and Velma L. Chandler. 39: 340–344, Mar. 1949.

Stillbirths and mortality of prematures in Rumania. [Syphilis.] Public Health in Foreign Periodicals. 39: 405–406, Mar. 1949.

AM. J. SURG., NEW YORK

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Skin reaction of patients to Donovania granulomatis. Calvin H. Chen, Robert B. Dienst and Robert B. Greenblatt. 33: 60–64, Jan. 1949.

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The causes of blindness of twenty years ago and today. E. Redslob. 181: 535–543, Sept. 1948. [Abstracted in Am. J. Ophth., Chicago, 32: 620, Apr. 1949.]

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Penicillin in the treatment of gonococcal ophthalmia of the newborn and of septic endophthalmitis. (La penicilina en el tratamiento de la oftalmia gonocócica del recien nacido y en la endoftalmitis séptica.) E. Dalgado Benavides. 7: 1121, 1947. [Abstracted in Brit. J. Ven. Dis., London, 24 : 169, Dec. 1948.]

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Cutaneous manifestations of early syphilis. John Godwin Downing. 12 : 1–5, Jan. 1949.

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The medical profession and the Federal health grants. [V. D.] W. V. Johnson. Medical Economics. 60 : 301–304, Mar. 1949.

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Recent advances in the diagnosis and treatment of heart disease: A critical review. [Syphilis.] C. L. Tung. 66 : 622–628, Nov. 1948.

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Gonorrhea, enemy of mankind. Theodore Rosenthal. V. D. Part III. 27: 330–331, 359, May 1949.

J. A. M. A., Chicago

*The Jarisch-Herxheimer phenomenon in late syphilis. Probable fatal reactions to penicillin. Virgil Scott, Richard W. Maxwell and John S. Skinner. 139: 217–220, Jan. 22, 1949.

Survey of medical care among the Upper Midwest Indians. W. F. Braasch, B. J. Branton and A. J. Chesley. Special Article. 139: 220–226, Jan. 22, 1949.

Premarital examination for syphilis. Editorials. 139: 310–311, Jan. 29, 1949.

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Penicillin for oral prophylaxis of venereal disease—a warning. 139: 925, Apr. 2, 1949.

Primer on the rheumatic diseases. Prepared by a committee of the American Rheumatism Association. [V. D.] 139: 1068–1076, Apr. 16, 1949; 1139–1146, Apr. 23, 1949; and 1268–1273, Apr. 30, 1949.

The Jarisch-Herxheimer phenomenon in late syphilis. Probable fatal reactions to penicillin. Virgil Scott, Richard W. Maxwell and John S. Skinner. J. A. M. A., 139: 217–220, Jan. 22, 1949.

The authors present the case reports of two patients with late syphilis who died shortly after the institution of penicillin therapy. The evidence in one patient, with a proved gumma of the brain, who died suddenly and unexpectedly 14 hours after the initial injection of penicillin, offers convincing proof of the occurrence of a fatal Jarisch-Herxheimer reaction. This fatality represents the first reported, to date, following the administration of penicillin. In the other patient, with an aortic aneurysm which ruptured 49 hours after the institution of penicillin, the evidence in favor of a fatal Herxheimer reaction is suggestive.

The condition of the first patient, a 21-year-old white housewife, had not been considered critical. She was seriously ill and there had been no favorable progress during 10 days of observation. Of crucial importance from the standpoint of substantiating the occurrence of a Herxheimer reaction was the elevation of body temperature to 38.1° C. (100.6° F.) 6 hours after the first injection of 60,000 units of crystalline G sodium penicillin and 8 hours prior to death. At the time of admission the rectal temperature was 37.2° C. (99° F.). This was the only elevation in temperature recorded during the entire 11 days of hospital observation. Thirteen hours after the first injection the patient had a generalized convulsion, and 1 hour later was found dead.

A review of the literature indicates that there have been a small number of reported serious reactions considering the many thousands of patients who have been treated with penicillin.

The authors conclude that the prevention of Herxheimer reactions requires further study. In gumma of the larynx and of the brain, where Herxheimer reactions may be fatal, probably in dementia paralytica and in primary optic atrophy, and perhaps in cardiovascular syphilis, attempts at prevention should be considered.

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J. Am. Pharm. A. (Prac. Pharm. Ed.), Easton

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J. Am. Pharm. A. [Scient. Ed.], Washington

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The serum concentration of penicillin G in mice, rabbits, and men after its intramuscular injection in aqueous solution. Harry Eagle, Ralph Fleischman and A. D. Musselman. 57: 119–126, Jan. 1949.

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A chemical determination of streptomycin in body tissues and urine. Viola C. Jelinek and George E. Boxer. 175: 367–375, Aug. 1948.

J. Bone & Joint Surg., Boston

Bone and cartilage debris in the synovial membrane. Its significance in the early diagnosis of neuro-arthropathy. [Tabes.] Thomas Horwitz. 30–A: 579–588, July 1948.

J. Bone & Joint Surg., London

Recurrent dislocation of the shoulder. Lesions discovered in seventeen cases, surgery employed, and intermediate report on results. [Syphilis.] A. L. Eyre-Brook. 30–B: 39–48, Feb. 1948.

Atlas of general affections of the skeleton. 3. Melorheostosis. [Syphilis.] H. A. Thomas Fairbank. 30–B: 533–543, Aug. 1948.

Arthroplasty of the knee joint. Late results. [Gonorrhea.] J. Edouard Samson. 31–B: 50–52, Feb. 1949.

Arthroplasty of the knee. A follow-up study. [Gonorrhea.] J. S. Speed and Philip C. Trout. 31–B: 53–60, Feb. 1949.

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Use of blood donors with positive serologic tests for syphilis—with a note on the disappearance of passively transferred reagin. Mark M. Ravitch, Thomas W. Farmer and Barbara Davis. 28: 18–23. Jan. 1949.

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Some safeguards in antibiotic therapy with special reference to penicillin and streptomycin. Joseph Farrington and J. Frank Wilson. 35: 497–500, Feb. 1949.

Venereal diseases; diagnosis and treatment. Roger F. Sondag. 35: 699–703, May 1949.

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J. Indiana M. A., Indianapolis

Why malaria cures general paralysis. Walter L. Bruetsch. 42: 211–216, Mar. 1949.

J. Invest. Dermat., Baltimore

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*The treatment of asymptomatic neurosyphilis in the white mouse. Harold J. Magnuson and Barbara Rosenau. 11: 435–441, Dec. 1948.

Serum concentrations following five treatment schedules with procaine penicillin in oil with aluminum monostearate. D. K. Kitchen, E. W. Thomas and C. R. Rein. 12: 111–115, Feb. 1949.

The treatment of asymptomatic neurosyphilis in the white mouse. Harold J. Magnuson and Barbará Rosenau. J. Invest. Dermat., 11: 435–441, 1948.

The authors present a report of investigations in which they have employed asymptomatic central nervous system syphilis in white mice for the therapeutic assay of penicillin, mapharsen, and tryparsamide.

The first attempts to produce this central nervous system infection in white mice met with irregular success. Preliminary investigations which were undertaken to resolve these irregularities are described in detail. As a result of these studies the authors found that the size of the inoculum and the duration of the infection are both related to the development of the central nervous system infection.

Following these preliminary studies, therapeutic assays were made on the central nervous system infection in 116 mice established by the intraperitoneal inoculation of 10^6 *Treponema pallidum* (Nichols strain) 3 months prior to treatment. Treatment consisted of either penicillin, mapharsen, or tryparsamide. The penicillin was given as penicillin G in peanut oil-beeswax in four daily subcutaneous injections. The mapharsen and tryparsamide were given in a single intraperitoneal injection. As a test of cure, 6 weeks after treatment the mice were exsanguinated and the mouse brains transferred to rabbits.

As a result of their investigations, the authors conclude that penicillin is the only drug showing therapeutic activity. At doses from 16,000 units per kilogram and upward, significant numbers of the mice were cured. The 50-percent curative dose may be estimated at approximately 14,000 units per kilogram, and the 90-percent curative dose at approximately 64,000 units per kilogram. With tryparsamide, doses up to 2,400 mg. per kilogram failed to cure significant numbers of the mice. With mapharsen, doses up to 36 mg. per kilogram were similarly unsuccessful. Since the maximum tolerated doses of tryparsamide and mapharsen are respectively 2,500 mg. per kilogram and 34 mg. per kilogram, these drugs as here used would have no therapeutic value.

The authors state that it is not known whether the 6 weeks' interval allowed between the termination of treatment and transfer as a test of cure is adequate. It may be that some of the animals apparently cured by penicillin would not have been so cured had transfer been carried out at a later date. Such delayed transfers are in the process of study. Regardless of the reliability of the present method as an absolute criterion of cure, the relative effectiveness of the three drugs is clear.

In conclusion, the authors review the literature and present a discussion of the observations of other workers as compared with findings herein reported.

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New penicillin products for sustained effects. Leo Loewe, Albert E. Sobel and Erna Alture-Werber. 34: 67–73, Jan. 1949.

Blood and cerebrospinal fluid concentrations of aureomycin after oral and intramuscular administration. Mark H. Lepper, Harry F. Dowling, Robert L. Brickhouse and Eston R. Caldwell, Jr. 34: 366–371, Mar. 1949.

The excretion of penicillin in human milk. R. Rozansky and A. Brzezinsky. 34: 497–500, Apr. 1949.

J. M. A. Alabama, Montgomery

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J. M. A. Eire, Dublin

A case of arsenical dermatitis treated with B. A. L. John J. Gray. 23: 38–39, Sept. 1948.

J. M. A. Georgia, Atlanta

Management of acute gonorrhea. Fenwick T. Nichols, Jr. Georgia Department of Public Health. 38: 35–37, Jan. 1949.

J. M. Soc. New Jersey, Orange

Decrease in the attack rate of syphilis. A. J. Casselman. 46: 32, Jan. 1949.

Acridine-sulfonamide therapy of trichomonas vaginitis. Robert A. Cacciarelli. 46: 87–88, Feb. 1949.

The therapeutic test: a neglected diagnostic tool. [Syphilis.] Sidney Friedenberg. 46: 130–132, Mar. 1949.

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J. Ment. Sc., London

Psychiatric hypothesis and practice. [Syphilis.] David Henderson. 94: 18–32, Jan. 1948.

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Histopathological findings in general paresis after penicillin treatment: report on four cases. Robert H. F. Smith and Vamberto de Morais. 94: 70–76, Jan. 1948.

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J. Michigan M. Soc., St. Paul

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Angina of effort in pregnancy. (Report of a case.) [Syphilis.] A. Schott. 55 : 428–431, Aug. 1948.

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The acute joint. William K. Ishmael. 42 : 11–14, Jan. 1949.

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J. Pediat., St. Louis

Pediatric deaths in a large general hospital. [Syphilis.] R. V. Platou, John Kometani and Norman C. Woody. 32 : 380–392, Apr. 1948.

An evaluation of the penicillin treatment in early congenital syphilis. Leslie Paxton Barker. 32 : 516–521, May 1948.

Relationship of race to the incidence of diphtheria and to Schick, tuberculin, and Wassermann tests in hospitalized children. David W. Martin and Jay M. Arena. 32 : 530–531, May 1948.

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Competitive health preservation in the army. [VD] F. M. Richardson. 91 : 203–218, Nov. 1948.

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Psychiatric factors in social hygiene problems. Editorial. 35 : 7–8, Jan. 1949.

Social hygiene—a psychiatric viewpoint. Brian Bird. 35 : 9–19, Jan. 1949.

A psychiatric approach to the treatment of promiscuity. Benno Safier et al. 35 : 20–25, Jan. 1949.

The venereal disease patient as a delinquent. Leslie E. Luehrs. 35 : 26–33, Jan. 1949.

New approaches to old objectives. Annual report of the American Social Hygiene Association for the year 1948. Walter Clarke. 35 : 51–74, Feb. 1949.

News from the States and communities. [Syphilis in food handlers.] Esther Emerson Sweeney. 35 : 87–89, Feb. 1949.

New educational methods and materials. VD education at seven Michigan Fairs. 35 : 94–95, Feb. 1949.

A new day for health and welfare. [V. D.] Frances Payne Bolton. 35 : 104–109, Mar. 1949.

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Urethral stricture: a pathological study. [Gonorrhea.] Donald E. Beard and William E. Goodyear. 59 : 619–626, Apr. 1948.

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Neurofibroma of tunica albuginea testis. [VD] Benjamin Levant and Milton A. Chetlin. 59 : 1187–1189, June 1948.

Transurethral resection for neurological bladder. [VD] John E. Dees. 60 : 907–914, Dec. 1948.

*Treatment of acute uncomplicated gonococcal urethritis with a single dose water-soluble penicillin preparation. Leo Loewe, Theodore Rosenthal, William Leifer, Perry Katzen, Harold B. Eiber and Sidney Cohen. 60 : 958–963, Dec. 1948.

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Treatment of acute uncomplicated gonococcal urethritis with a single dose water-soluble penicillin preparation. Leo Loewe, Theodore Rosenthal, William Leifer, Perry Katzen, Harold B. Eiber and Sidney Cohen. J. Urol., 60: 958–963, 1948.

The authors present a report of the treatment of acute uncomplicated gonococcal urethritis in 142 male patients at the Jewish Hospital of Brooklyn, using a single injection of dehydrated, water-soluble, penicillin-gelatin preparation. The pharmacology of this preparation is discussed.

A single, conventional dose of 300,000 units of penicillin in the gelatin-dextrose mixture was administered to the first 52 patients of the series as a shallow intramuscular deposit in the thigh. The remaining 90 patients, because of ease of administration and absence of local reaction, and as a time-saving device in the ambulatory subject, received the injection in the deep subcutaneous tissues of the posterior aspect of the upper arm.

Exploratory penicillin blood assays were done from time to time primarily to check the potency of the penicillin gels used in this study. Patients were ordered to report weekly for a period of three successive weeks after treatment. To prevent masking of a coexistent syphilis, patients were told to have a serologic test for syphilis monthly, for a period of at least 4 months.

Fourteen patients in the series were lost from observation. Of the 128 suitable for statistical survey, 3 (2.4 percent) were considered failures, 2 (1.5 percent) were classified as probable reinfections, while 123 (96.1 percent) were satisfactory. The term "satisfactory" is used to connote clinical and bacteriologic "cure." Of the 3 patients who were considered treatment failures, 2 were later cured by intensive re-treatment.

There were no toxic manifestations; only two patients had local, transitory soreness and swelling. No instance of urticaria was observed nor were any other allergic phenomena reported. This record may be ascribed to the nonallergenic property of gelatin and the anti-allergic influence of the vasoconstrictor drugs in the preparation.

Twenty-six of the infecting organisms in this series were processed for penicillin sensitivity. The values were unexpectedly high, ranging from 0.004 to 0.25 Oxford units per milliliter of test broth for bacteriostasis, and 0.008 to 0.5 Oxford units per milliliter of test broth for the minimal lethal doses. No correlation was found between penicillin sensitivity and treatment failure. Rather, the percentage of successes in this series may be attributed to the concentration and duration of penicillin levels in the blood. Penicillin assays of blood disclose measurable levels up to 24 hours following a single injection of 300,000 Oxford units in the gelatin-dextrose preparation. The average blood penicillin levels are at peak during 8 to 13 hours (0.08 to 1.91 Oxford units per milliliter) and then taper off to a level (0.015 Oxford units per milliliter) which is still bacteriostatic for many strains of gonococci. The peak levels, which persist for 8 to 13 hours, are sufficient for minimal lethal dosage purposes for even the most resistant strains of organisms encountered in this series.

The results of this study compare favorably with any previously reported series conducted in a similar manner.

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Oral aureomycin in the therapy of streptomycin-resistant granuloma inguinale. Robert B. Greenblatt, Robert B. Dienst, Calvin Chen and Robert West. South. M. J., 41: 1121–1123, 1948.

This is the first report on patients with streptomycin-resistant granuloma inguinale who were treated with a new antibiotic, aureomycin.

Streptomycin-resistant cases were encountered which failed to respond to several intensive courses of streptomycin covering periods up to 10 days utilizing doses up to 40 gm. of the drug with each course. Some of these patients had failed to respond to antimonials and to every other form of therapy attempted. At first, aureomycin in doses of 20 mg. per day parenterally was tried. No response was obtained. The dosage was then increased to 20 mg. every 4 to 6 hours for periods of from 7 days to 3 weeks, and again the lesions failed to heal. Oral aureomycin was then instituted, and the response to oral therapy was dramatic.

Case histories of four patients treated with oral aureomycin are presented. The first was treated 14¼ days with 250 mg. administered four times a day for a total of 14,250 mg. until healing was complete. The second, third, and fourth patients were treated for 5 days, with 250 mg. four times a day each for a total of 5,000 mg. Two of these three healed completely but in the last and most extensive case there remained a small area in which occasional Donovan bodies, mostly in a degenerative stage, could be found. This patient is receiving a further course of oral aureomycin with satisfactory results to date. No untoward toxic reactions were noted in these patients.

The authors conclude that a dose of 5,000 mg. is sufficient for the moderate case of granuloma inguinale but that in those cases in which lesions are extensive, the therapy should be continued until healing is complete.

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Reported Civilian Venereal Disease Cases and Rates per 100,000 Population, Continental United States, Fiscal Year 1948

Disease and stage	Number of cases reported						
	Total	White			Nonwhite		
		Total	Male	Female	Total	Male	Female
Total syphilis	338, 141	127, 210	70, 139	57, 071	210, 931	94, 112	116, 819
Primary or secondary	80, 528	33, 215	20, 169	13, 046	47, 313	24, 135	23, 178
Early latent	97, 745	26, 673	11, 821	14, 852	71, 072	26, 709	44, 363
Late and late latent	123, 972	49, 873	28, 499	21, 374	74, 099	34, 922	39, 177
Congenital	13, 309	5, 348	2, 157	3, 191	7, 961	3, 556	4, 405
Stage not reported	22, 587	12, 101	7, 493	4, 608	10, 486	4, 790	5, 696
Gonorrhea	363, 014	123, 563	82, 588	40, 975	239, 451	171, 359	68, 092
Chancroid	8, 631	2, 179	1, 966	213	6, 452	5, 283	1, 169
Granuloma inguinale	2, 315	105	80	25	2, 210	1, 305	905
Lymphogranuloma venereum	2, 494	205	172	33	2, 289	1, 760	529
	Rates per 100,000 population						
Total syphilis	234. 5	98. 7	110. 2	87. 5	1375. 5	1256. 5	1489. 1
Primary or secondary	55. 8	25. 8	31. 7	20. 0	308. 5	322. 2	295. 4
Early latent	67. 8	20. 7	18. 6	22. 8	463. 5	356. 6	565. 5
Late and late latent	86. 0	38. 7	44. 8	32. 8	483. 2	466. 2	499. 4
Congenital	9. 2	4. 2	3. 4	4. 9	51. 9	47. 5	56. 2
Stage not reported	15. 7	9. 4	11. 8	7. 1	68. 4	64. 0	72. 6
Gonorrhea	251. 8	95. 9	129. 7	62. 9	1561. 5	2287. 8	868. 0
Chancroid	6. 0	1. 7	3. 1	. 3	42. 1	70. 5	14. 9
Granuloma inguinale	1. 6	. 1	. 1	. 0	14. 4	17. 4	11. 5
Lymphogranuloma venereum	1. 7	. 2	. 3	. 0	14. 9	23. 5	6. 7

Source: Reported cases from US PHS Form 8958–B. Total civilian population estimate for January 1, 1948—Bureau of the Census, Current Population Reports P–25, No. 13, August 13, 1948. Color and sex civilian population estimates for January 1, 1948—Bureau of the Census, unpublished data.

FSA—PHS—Division of Venereal Disease, Office of Statistics, 6/14/49 (ML–MJB) mw.

NOTE: A similar table for fiscal year 1947 appears in THE JOURNAL OF VENEREAL DISEASE INFORMATION, January 1948, vol. 29, No. 1, page 29.

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The JOURNAL *of* VENEREAL DISEASE INFORMATION

Volume 30 September 1949 Number 9

EDITORIAL
Congenital Syphilis 241
ORIGINAL ARTICLES
A Study of Nonspecific Urethritis in British Soldiery 243
R. R. Willcox, M. B.
Penicillin in the Abortive Treatment of Syphilis 252
Frederick Plotke, M. D., M. P. H.
Henry Eisenberg, M. D.
Amelia H. Baker, M. A.
M. E. Laughlin, M. S., Statistician
The Baffling Case of Baby T 257
E. Walter Shervington, M. D.
Cornelia M. Phillips, R. N.
N. A. Nelson, M. D.
CURRENT NOTES AND REPORTS 260
CURRENT LITERATURE 263
STATISTICS
Cases of Congenital Syphilis Reported to the Public Health Service, Fiscal Years 1941–49, by Quarters 273

FEDERAL SECURITY AGENCY
Public Health Service

52. 9

Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

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PUBLIC HEALTH SERVICE
Leonard A. Scheele, *Surgeon General*

Editor: THEODORE J. BAUER, *Medical Director*
Chief, Division of Venereal Disease

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Editorial

Congenital Syphilis

In a previous editorial we discussed the decline in morbidity reporting of primary and secondary syphilis and stated that this probably represents a decline in the incidence of syphilis. What, then, is the meaning of the number of cases reported as congenital syphilis, which has remained constant for the past 5½ years, during the period when the use of penicillin became widespread? Penicillin is the most effective treatment yet utilized for syphilis in pregnancy; therefore, to the extent that pregnant women are treated, we should expect the number of babies being born with syphilis to decrease. Moreover, if there is a reduction in the incidence of syphilis, we should expect fewer pregnant women to be infected with syphilis.

Does the constant level of morbidity reporting of congenital syphilis mean that there has been no decrease in the incidence of congenital syphilis, or does it mean that consistent improvement in case finding has offset a possible decrease in incidence, thus keeping the reporting at a constant level? We do not know. We do know, however, that over the past 11 years there has been a continuous decrease in the infant mortality rate from syphilis, which has continued into 1948. It would seem reasonable to assume that the total congenital syphilis rate among live births decreased in a similar fashion, but morbidity reporting does not support this assumption.

Of one thing we are sure. There is too much congenital syphilis, and too much of it goes untreated into the later years of life. Only one-fifth of the congenital syphilis reported is found in children under 1 year of age, with four-fifths going into later years; most cases are not discovered until elementary school or high school. Many will say that much of the congenital syphilis reported as found in older children and adults is in fact acquired syphilis. Still, only 26 percent of the congenital syphilis discovered in children 14 years of age or younger is being discovered before the first year of life.

To what can we attribute our lack of case finding of congenital syphilis in the first years of life? In studies made by the Division we find that most congenital syphilis discovered in older children could have been found earlier. In many instances the mother had been treated for syphilis, but her children (exposed to the infection in utero) were not examined. Some of this neglect is attributed to the emphasis placed in recent years on the case finding of primary and secondary syphilis. It is stated that so much emphasis has been placed on the sexual contacts of early infectious syphilis that the children have been neglected. It is true we have recommended that sex contacts of primary and secondary syphilis patients should get priority and that only children exposed to the lesions or in utero need be examined. But it is not among the children of women with primary and secondary syphilis that most congenital syphilis is found. Only the younger infants of mothers with primary and secondary syphilis could possibly get congenital syphilis from this infection. *It is in the children of women with latent syphilis that congenital syphilis is to be found.*

Successful prevention of congenital syphilis begins during pregnancy. Much congenital syphilis can be prevented if public health workers will see that all mothers under their supervision have at least one blood test during pregnancy, and preferably two. A positive blood test in a pregnant mother constitutes a medical emergency, and no time should be lost in securing adequate diagnosis and treatment. It is realized that in some sections of the country many mothers are not able to have medical care and depend in many instances upon assistance from midwives. It is extremely important that all such mothers have a blood test before the baby is born; if this is not possible, public health workers' efforts should be applied to seeing that the mother has a blood test at delivery or very soon afterwards. In this way it is possible to locate congenital syphilis early, when treatment is apt to be more successful.

For those children whose congenital syphilis has not previously been discovered, it is suggested that careful screening examinations of school children, including a blood test, be made in areas of high prevalence. Moreover, it has been shown that screen dental examinations of school children are effective in locating late congenital syphilis and may be profitable as a case-finding technic in high prevalence groups.

However, any age is too late to find congenital syphilis; it *is* preventable. We have the treatment; we should have the case-finding mechanism to find pregnant women with syphilis. Every case of congenital syphilis is a failure of syphilis control.

THEODORE J. BAUER, *Medical Director*
Chief, Division of Venereal Disease

A Study of Nonspecific Urethritis in British Soldiery

R. R. Willcox, M. B.[1]

Introduction

The distressing and little understood condition of nonspecific urethritis only finally threw off its confusing mantle of gonorrhea during World War II as thousands of early morning smears taken from its sufferers in the military hospitals were examined for the gonococcus and found wanting—for prior to this the gonococcus, even if not found, was still believed by some to be the motivating cause. For example, although McElligott (*1*), in a paper read during 1942 before the Medical Society for the Study of Venereal Diseases, London, expressed no doubt as to the individuality of the disease, records of the subsequent discussion indicate that others present certainly considered the gonococcus to be responsible for an appreciable number of cases.

Since this time the disease has been given closer attention and for some years now has been well recognized. Of 2,000 American troops serving in the Pacific theater, for example, 2.97 percent had contracted a gonococcic infection, whereas 12.4 percent had a nonspecific urethritis (*2*). Its possible and occasional causes are legion but, when those cases due to chemical irritation, crystalluria, prostatorrhea, trichomonads, spirochetes, amebae, trauma, intraurethral sores, foreign bodies and tumors, cystitis from all causes, long-standing gonorrhea, and urethral stricture have been excluded, we are left with a large residue which forms the disease as we know it today. It is customary to divide this further into bacterial and abacterial urethritis: the former being associated with demonstrable micro-organisms, particularly *Bacillus coli,* while, for the latter, trichomonads have been claimed as responsible for a proportion of cases by some (e. g., Fieldsend (*3*)), spirochetes by some (e. g., Coutts (*4*)), and a virus by others (e. g., Harkness (*5*)), while of recent years it has been more fashionable to blame members of the pleuropneumonia-like group. Harkness and Henderson-Begg (*6*) found these organisms present in 26 of 67 cases, although Salaman (*7*) claimed that they were commonly associated with the gonococcus.

Ordinary cultures of the discharges grow a variety of organisms, which, for the most part, are saprophytes and unassociated with the disease. Weckstein (*8*) found a urethral *Staphylococcus albus* in 68.3 percent, and in the vast majority the organisms were resistant in vitro to penicillin, neoarsphenamine, and sulfadiazine.

Clinically, the disease responds to sulfonamides to some appreciable extent, but it was only after the introduction of penicillin, which was to prove so final for gonorrhea but at the same time useless for nonspecific urethritis, that the disease came to be thrown into even more definite relief; a possible (but not recommended) method of differentiating the condition from gonorrhea is to give a dose of penicillin and observe the result. Indeed, when reading the literature, one feels that the disease was largely unrecognized even later in the United States than in Britain, and it was only after the wide use of penicillin for gonorrhea and the later critical examinations of so-called penicillin failures (as by Parkhurst et al. (*9*) that its very existence received Nation-wide acknowledgment.

At the present time the treatment of the complaint is likely to be revolutionized by the antibiotics. Penicillin being ineffectual, it is only latterly that other preparations are being tested. Streptomycin is effective in vitro against pleuropneumonia-like organisms, and reports of its effectiveness in nonspecific urethritis are coming in (*10, 11, 12*), while aureomycin also appears to be effective to some degree (*13*), a fact confirmed in a pilot study by the author (*14*).

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[1] Physician in Charge, Venereal Diseases Department, King Edward VII Hospital, Windsor, England; Senior Assistant Medical Officer, Venereal Diseases Department, St. Mary's Hospital, Paddington, London, England; formerly Adviser in Venereology to the War Office; at present Adviser in Venereology to the Government of Southern Rhodesia.

This study concerns British soldiery stationed in London and the Home Counties during July through October 1943, who were treated as in-patients at a military hospital in the London area. Originally 100 men were subjected to special questioning in order to try to elicit collateral data which it was hoped might help to penetrate the cloud of mystery, now perhaps a little thinner, which then surrounded the condition. Gonorrhea was later considered to have been responsible for 14 of the cases, and these were excluded from the series. Fifty other nonvenereal patients admitted at the same time to the same hospital for nonvenereal skin complaints (such as psoriasis, impetigo, dermatitis, epidermophytosis, urticaria, sycosis, eczema, and seborrheic dermatitis) acted as controls. Those with scabies were deliberately excluded.

I. Habits

Personal Background

The average age of the 86 venereal patients was 27.75 years and that of the 50 skin patients 27.2 years. Regarding length of service, 15.1 percent of the venereal and 18.0 percent of the control group had served for less than 1 year, and the average length of service for the two groups was 2.3 and 2.4 years, respectively. As regards marriage, 50 (58.2 percent) of the venereal group were married, as were 27 (54 percent) of the control group. The average duration of marriage for the married members of the 2 groups was 4.8 and 5.4 years, respectively. Ten (20 percent) of the venereal group were childless so far, 32 percent had 1 child, 26 percent 2 children, 10 percent 3 children, and 12 percent 4 or more children. A lesser libido in the control group might be inferred when it is noted that 61 percent of the marriages were childless so far; 19 percent had 1 child; 8 percent, 2 children; 8 percent, 3 children; 4 percent, 4 children; and none had more than this number.

Five of the venereal patients had been the only child; there was an average of 4.08 brothers and sisters per patient in this group. Three of the controls had been the only child; the brothers and sisters averaged 4.54 per patient. Thus, in the family background of the two groups, there were few differences apart from the numbers of offspring: the venereal patients were the more fruitful.

Previous History

This was probed from three angles: (1) previous venereal complaints, genitourinary illnesses, and trauma; (2) personal and family history of allergy; and (3) psychological disturbances.

Urologic Factors

Forty-five of the 86 urethritis patients had had 53 previous attacks of venereal disease (gonorrhea, 22; nonspecific urethritis, 24; syphilis, 2; epididymitis, 2; balanitis, etc., 3). *Thus, 52.3 percent were already venereally scarred at the time of the present attack.* These figures are in accord with those of Price (*15*), who noted that, of 99 patients with nonspecific urethritis attending two London hospitals, no less than 42 had previously had gonorrhea. In addition, 5 of the present series gave a history of backache; 2 complained of an inability to hold their urine; 1, of varicocele; 2 had nephritis; and 11 gave a history of genitourinary trauma varying from kicks in the testicles to rupture of the urethra and fracture of the pelvis; in 7 instances, however, they occurred more than 4 years previous to the present disease. One had hypospadias and 2 a "pin-hole" urinary meatus.

In the control group, only four (*8 percent*) *gave a history of previous venereal disease* (two, gonorrhea; one, syphilis;

and one, urethritis); one gave a history of injury to the testicle in an accident the year before.

Allergic Factors

Two of the urethritis group gave a history of urticaria, 4 of hay fever, 4 of rhinorrhea, and 1 of asthma (total 11, or 12.8 percent). Five of these 11 also suffered from migrainous and other headaches. The family histories were likewise largely negative, only one patient having a brother who suffered from asthma.

In the control group, one suffered from asthma, one from hay fever, one from rhinorrhea, and one from urticaria (total four, or 8 percent).

Psychological Factors

The psychological aspects of nonspecific urethritis are not without interest, for the disease certainly seems to attack an undue proportion of sensitive neurotic patients. Although it may be that such persons are more prone to observe a condition which perhaps may pass unnoticed in a more phlegmatic individual, it is probably only evidence of the psychological imbalance of which the contraction of venereal disease is but a symptom.

The difficulties in making a convincing evaluation of such matters are notorious, for there are few criteria which are not open to criticism. The factors chosen were as follows:

1. A history of previous treatment at the hands of a psychiatrist, or a history of nervous breakdown (this factor was considered of most value).
2. A family history of insanity or reference to a psychiatrist (also considered of great value).
3. Excessive worry (this is open to the objection that the patients were men away from their homes while their wives and families were in danger of air attack, although, to be fair, the air raids were at a much reduced level at the time this survey was undertaken).
4. Insomnia.
5. Excessive sweating (the men, it must be remembered, wore battle dress and Army socks and boots, and this form of clothing was often uncomfortably warm under summer conditions; it should not be forgotten, either, that in the Army the term "sweating" also means "worried").
6. Tremor of the outstretched hand (this sign was of some value, as only the most nervous would still show tremor by the time the questioning was completed).
7. Stuttering.
8. Introspection, as evidenced by an excessive elaboration of previous and present complaints (noted only when marked).
9. Weeping or undue depression at the time of examination (noted only when marked).
10. A history of train sickness.
11. A history of recurrent headaches.

Of the 86 patients of the *urethritis group*, 56 (65 percent) admitted to having one or more of these symptoms (table 1). Twenty-four had only one symptom; 32, two or more; 17, three or more; and 10, four or more. It is noted that no less than 29 (33.7 percent) complained of headaches. Of these, 11 were of a migrain-

Table 1.—*Psychological disturbances*

Symptom	Urethritis group (86 cases)		Skin group (50 cases)	
	Number of patients	Percentage of patients having symptom	Number of patients	Percentage of patients having symptom
Previous psychiatric treatment	12	14.0	3	6.0
Family psychiatric treatment	11	12.8	2	4.0
Excessive worry	24	27.9	7	14.0
Insomnia	2	2.3	------	------
Excessive sweating	23	26.6	9	18.0
Tremor	9	10.5	4	8.0
Stutter	1	1.2	------	------
Introspection	9	10.5	1	2.0
Weeping or depression	3	3.5	2	4.0
Train sickness	1	1.2	------	------
Headaches	29	33.7	11	22.0
Total number of symptoms reported	124	------	39	------
Patients affected	56	65.0	23	46.0

ous nature, being paroxysmal, unilateral, and often accompanied by vomiting, while two others had suffered from migraine at an earlier age. Five also complained of occasional headaches. Of the remainder, 3 followed head injuries, 4 were of a frankly functional nature, 2 were associated with eyestrain, 1 with the ears, and 1 with the sinuses.

The incidence of mental upset, however, was not low in the *control group*. This group was composed of skin patients who, in any case, were likely to show some psychological disturbances. Of the 50 patients, 23 (46 percent) reported 39 symptoms; 11 had only one; 12, two or more; 5, three or more; and 1, four or more. It is evident, however, that all of these figures portrayed in table 1 are substantially lower than those of the urethritis group.

Sex Habits

Last Intercourse: Time Interval Prior to Admission (Table 2)

This is not a valid ground for comparison between the two groups, because the most recent intercourse was, for the urethritis group, usually responsible for the acquisition of the infection which brought the patient to the hospital.

It is noted that the incubation period of nonspecific urethritis is commonly from 4 to 21 days; also, that over one-third of the control group, married or single, had not indulged in sexual intercourse for over 2 months. Actually, only 6 of the 23 single men (26.1 percent) admitted having intercourse during this time.

Table 2.—*Number of days since last coitus*

	Urethritis group (86 patients)	Skin group (50 cases)
Denies coitus	0	6
Number of days since last coitus:		
1–3	3	0
4–7	29	4
8–14	17	6
15–21	13	3
22–28	4	3
29–35	4	3
36–42	2	1
43–49	1	0
50–56	4	6
Over 56	9	18
Total	86	50

Nature of Last Intercourse

Of the 86 patients in the urethritis group (50 of whom were married), only 24 of the contacts were marital. Eighteen of the contacts were female friends, and no less than 44 were feminine strangers. There were no homosexuals. Of the 44 intercourses with strangers, 32 (72.7 percent) took place out-of-doors. Of the 18 with friends, only 6 (33.3 percent) took place in the open air. (The "black-out" was in operation at the time.)

Of the 50 patients of the control group (27 of whom were married), the most recent intercourse was with the wife in 25 cases, with a friend in 17, and with a stranger in only 2. Six denied ever having had intercourse, although 1 of these gave a history of previous urethritis.

Position.—In the urethritis group, the last intercourse had been conducted in the "normal" position in 67 instances, with the female partner lying face upwards with the male on top. In 2 instances it was side by side (face to face in one, and front to back in another—the wife being pregnant); and in 17 (15 with strangers and 2 with friends), it was performed in the standing position. In the control group, one married man described it as "various," but for the rest it was normal.

Urination.—Of the urethritis group, 58 (67 percent) passed urine soon after the act and 28 did not; 22 (44 percent) of the controls admitted to passing urine within a few minutes after intercourse.

Last menstrual period of the female.—Of the 24 of the urethritis group having marital intercourse, 16 were cognizant of the menstrual history of the wife. Of the 18 having coitus with friends, 7 were also cognizant, but 42 of the 44 contacting strangers were not. In the 25 instances in which the menstrual history was known, the periods were absent in 6 (5 pregnancy and 1 lactation), in progress in 2, just over in 10, 2 weeks over in 4, and 3 weeks over in 3. These figures are probably not significant, as it is only a recent menstruation which is likely to be remembered.

In the control group, doubtless on account of the longer time interval since the event, only three married men could recall their wives' menstrual history. One wife was pregnant, and in the other two the period was just over.

Contraceptives. — In the urethritis group, a condom was worn by 11 men (3, wife; 4, friend; and 4, stranger); chemical contraceptives were employed by 2 (1, wife; 1, friend); and a Dutch-cap pessary was worn by 1 friend. Thus, in 62 extramarital intercourses, contraceptives were used only in 10.

In the control group a condom was worn by 8 (3, friend; 1, stranger; and 4, wife), and 3 married partners employed chemical means. Thus, only 4 of 19 extramarital intercourses were protected against pregnancy.

Prophylactics.—Apart from those of the urethritis group using a condom, 4 others employed the "E. T." prophylactic packet alone, as did 2 who had already used a condom. Only 8 of 44 intercourses with strangers were protected against venereal disease. Of the 2 of the control group having intercourse with strangers, 1 used a condom.

That this general lack of caution was exceptional and was responsible for the acquisition of nonspecific urethritis is belied when the precautions taken during the intercourse previous to the one studied are noted. Of 80 contacts, 15 used a condom (8, wife; 3, friend; 4, stranger), and only 7 of 38 extramarital intercourses were protected against pregnancy. Of 28 having intercourse with strangers, 1 employed a prophylactic packet and 4 a condom: thus, only 5 of 28 took advantage of venereal prophylaxis.

Evidence of Promiscuity: Previous Intercourse

Of the 23 single men of the control group, only 5 could give a reliable detailed history of the last intercourse but one. All intercourse was denied by 6; 12 had a "regular friend" or fiancée; 3 had had one or two intercourses with friends and 2 with prostitutes. If the adoption of a "regular friend" be considered normal, there was no general evidence of promiscuity.

Of the 86 in the urethritis group (50 married), 6 denied intercourse other than the one which brought the patient to the hospital; in 42, the last intercourse but one was with the wife; in 28, with strangers; in 10, with friends. It was a different person to the one that followed in no less than 44 cases (51.1 percent) and the same in 36 cases. In 34 instances, it took place less than 1 month prior to admission to the hospital; in 52, less than 2 months; and in 28, more than 2 months.

Except for 5 standing intercourses (3 with strangers and 2 with friends) and 1 in the sitting position with a stranger, all adopted the "normal" posture. Only 13 could recall the menstrual status of the partner (12 marital and 1 friend): 5 were pregnant; 1 was lactating; in 4, the period was just over; in 2, over for 1 week; and in 1, was just due.

Thirty-four percent of the married men of the urethritis group and 11.1 percent of the control group had been unfaithful to their wives.

Summary and Conclusions

1. Eighty-six patients with nonspecific urethritis have been studied as to their sexual habits and past history of urologic, allergic, and psychological disturbance, as have 50 nonvenereal patients suffering from dermatologic complaints.

2. The patients in the urethritis group were appreciably more active sexually than were those in the control group, as evidenced by the greater number of their children in a shorter period of married life, their promiscuous behavior, and the incidence of previous venereal disease. Of the urethritis group, 52.3 percent had had venereal disease prior to admission, as against only 8 percent of the controls.

3. Although there were no gross differences in allergic susceptibility, the patients of the urethritis group were psychologically disturbed to a greater degree than the controls. This is more

likely to be evidence of the psychological state of promiscuous persons as a whole than to be related to the disease.

4. Fifty-one percent of the urethritis group had had intercourse with two or more different persons in the previous 2 months. No less than 22 of the 36 single men of this group admitted to intercourse with a stranger on the occasion of the intercourse prior to the one that was responsible for their admission to the hospital, and 34 percent of the married men had been unfaithful to their wives.

In the control group, only two admitted that the last intercourse was with a stranger, and only 11.1 percent had been unfaithful to their wives.

5. There was insufficient evidence to say whether the urethritis was related to the menstrual history of the partner. Injections of citrated whole blood from the patients themselves or from other persons failed to provoke a discharge in 11 recently cured persons.

6. Neither the patients of the urethritis group nor of the control group indulged widely in contraceptive or prophylactic measures. Of 119 intercourses studied in both groups, contraceptives were used in only 21 instances (17.6 percent). Likewise, of 74 intercourses with strangers, only 14 (18.9 percent) were protected against venereal disease by condom or prophylactic packet.

II. Clinical

To the 86 patients discussed in part I of this paper are added a further 50 patients. The total of 136 cases, together with their response to treatment, are the subject of this clinical study.

Symptoms

The incubation period of the urethritis was commonly 4 to 21 days. Of the 136 cases, 8 had themselves noted no urethral discharge prior to admission to the hospital, but in 113 cases it had been present for periods up to a week and in 15 for longer than this time (in 83 cases it was for 4 days or less). Thirty-eight patients complained of dysuria (in 26 instances, for less than 7 days' duration), and 10 of these and 4 others complained of minor pains and irritation. Nine patients admitted to frequency of urination (in 7 instances, by day only), and 2 to urgency of urination.

Signs

The nature of the urethral discharge and the state of the urine are portrayed in table 3. Thus, 63 percent had a hazy urine and 37 percent did not. The disease was complicated in 7 by epididymitis, in 1 by acute prostatitis, in 2 by marked littritis, in 2 by tysonitis, in 1 by rheumatism, and in 1 by paraphimosis. Repeated early morning smears were taken while the patients were in the hospital in order to exclude the gonococcus. Urethral cultures were not performed in this series.

Table 3.—*Nature of the urethral discharge and of the urine*

	Number of patients	Percent
Nature of the discharge:		
Marked purulent discharge	32	23.5
Slight purulent discharge	5	3.8
Marked mucopurulent discharge	60	44.1
Scanty mucopurulent discharge	12	8.8
Mucoid discharge	16	11.7
Urethral moisture only	11	8.1
Total	136	100.0
Nature of the urine as adjudged by the 2-glass test:		
Hazy urine in 2 glasses	12	8.8
Hazy urine, first glass, with or without threads; second, clear	74	54.5
Clear urine: threads, first glass	21	15.4
Clear urine: specks, first glass	12	8.8
Clear urine, both glasses	17	12.5
Total	136	100.0

Treatment

Primary Treatment

The treatment schedules were various. Mandecal, a calcium mandelate compound in doses of 4.5 gm. 4 times daily without any auxiliary acidifying measures, was given to 20, urethral irrigations of 0.75 percent sodium bicarbonate to another 21, while 48 were given 24 to 42 gm. of sulfanilamide over a period of

4 to 7 days in conjunction with urethral irrigations. Eighteen others had sulfathiazole (24 gm. in 4 days) in conjunction with irrigations; 7 had sulfanilamide alone; 7, sulfathiazole alone; 10, sulfanilamide without irrigations but combined with 1 fever treatment induced by intravenous T. A. B. vaccine; and 5 had other treatment. A primary success is regarded as one in which no subsequent treatment was necessary. The results obtained are portrayed in table 4.

Table 4.—*Results of primary treatment*

Treatment	Number of patients	Successful treatment			Unsuccessful treatment		
		Average days of treatment	Number of successes	Percentage of successes	Number of relapses	Number of failures	Average days of treatment
No sulfonamides	42	---	21	50.0	3	18	---
Mandecal	20	6.22	8	40.0	1	11	18.63
Irrigations only	21	7.07	12	57.1	2	7	18.59
Vaccine and potassium citrate	1	9.00	1	---	---	---	---
Sulfonamides and irrigations	69	---	54	78.1	---	15	---
Sulfanilamide and irrigations	48	7 00	41	85.5	---	7	21.4
Sulfathiazole and irrigations	18	5.83	12	66.6	---	6	11.0
Sulfapyridine and irrigations	3	4.00	1	---	---	2	20.5
Sulfonamides alone	14	---	7	50.0	---	7	---
Sulfanilamide alone	7	7.40	5	71.4	---	2	17.0
Sulfathiazole alone	7	6.0	2	28.6	---	5	13.0
Sulfonamides and T. A. B	11	---	8	72.7	1	2	---
Sulfanilamide and T. A. B	10	7.75	8	80.0	---	2	22.5
Sulfathiazole and T. A. B	1	6.0	---	---	1	---	---
Total	136	---	90	66.2	4	42	---

Forty-two patients had no sulfonamides, with 18 failures and 3 relapses, a failure rate of 50 percent. Ninety-four had sulfonamides, with 24 failures and 1 relapse, a failure rate of 26.6 percent. Of the 65 patients receiving sulfanilamide, there were only 11 failures, a success rate of 85 percent. The figures for the sulfonamides were better when irrigations or fever were given in addition.

Sulfanilamide thus proved a fairly satisfactory preparation, and the results certainly compare favorably with those of King and Williams (*16*), who had 38 percent of primary successes in 98 patients given 45 gm. of sulfapyridine without irrigations over 14 days, and only 28 percent of primary successes with a further 98 patients given 23 to 25 gm. of sulfapyridine over 3 days, also without irrigations. In the present series, 65 were given sulfanilamide in the first instance. Fifteen received 42 gm. over 7 days, 11 had 36 gm. over 6 days, 9 had 30 gm. over 5 days, 25 had 24 gm. over 4 days, and 5 had 18 gm. over 3 days: the lesser amounts being dictated by clinical cure, or intolerance in a few cases. Complications of treatment included 1 case of severe vomiting, 3 of sulfonamide rash, and 1 of sulfonamide crystals in the urine but without hematuria or oliguria. By insuring that at least 10 pints of water were taken daily under military conditions, these were kept at a minimum.

Secondary Treatment

Forty-six patients required re-treatment. Similar lines of therapy were employed as at first, but each patient was given a type different than his previous therapy. In addition, urethral irrigations in 16 cases were combined with a course of mixed gonococcic vaccine given daily for 5 days, commencing with 100 million organisms and increasing by that

Table 5.—*Results of secondary treatment*

Treatment	Number of patients	Successful treatment			Number of failures
		Average days of treatment	Number of successes	Percentage of successes	
Total	46		31		15
No sulfonamides	30		21	70.0	9
Vaccine and irrigations	16	6.0	12	75.0	4
Misturia potassium citrate	1	5.0	1		
Irrigations only	13	8.0	8	61.5	5
Sulfonamides	16		10	62.5	6
Sulfanilamide only	7	4.8	5	71.4	2
Sulfanilamide and irrigations	3	5.5	2	66.6	1
Sulfanilamide and T. A. B	3	4.0	1		2
Sulfathiazole only	2	4.0	1		1
Sulfapyridine only	1	7.0	1		

amount with each dose. The results are portrayed in table 5.

Sixteen patients received sulfonamides (14 for the first time), with 10 successes (62.5 percent). Thirty had no sulfonamides, with 21 successes (70 percent). There is thus no evidence at this stage, when the natural course of the disease is one of quiescence, that sulfonamides were more successful than other measures.

Fifteen patients required a third treatment, during which eight were given sulfonamides, with two failures; three, irrigations only, with one failure; three, irrigations with vaccine in addition, with two failures; and one, with daily applications of sulfanilamide powder through the urethroscope, with success. Five patients required a fourth treatment, three a fifth, two a sixth, and one a seventh.

Duration in Hospital

Number of weeks spent in the hospital	*Number of patients*
1 or less	63
2 or less	113
2 to 3	12
3 to 4	4
Over 4	7

It will be noted that only 15 patients failed to 2 methods of treatment and that 121 responded (89.5 percent). Only 23 patients (16.9 percent) were in the hospital for more than 2 weeks.

Before discharge from the hospital, all patients were given a rectal examination, but, although a number were subsequently followed, the troop movements of the time rendered a systematic follow-up impossible.

All patients with epididymitis, and a number of others in addition, had a urine examination for the tubercle bacillus and had a blood examination for a gonococcic complement-fixation test. The results of these tests were negative.

Other Investigations

Cystoscopy

A cystoscopy was performed on 57 patients, usually on the fourth to the seventh day, either prior to discharge from the hospital in successfully treated cases or in resistant cases. Evidence of cystitis was present in 2 patients, doubtful evidence in 2, and a diverticulum of the bladder in 1. In the remaining 52 instances, nothing special was observed, and in no instance did the passage of the instrument aggravate the discharge or precipitate an epididymitis.

Injections of Blood Into the Urethra

In order to ascertain whether the presence of blood in the urethra would invoke a urethral discharge, seven patients had 3 cc. of their own citrated blood, and four others 3 cc. of citrated blood from another patient, injected into the urethra just prior to being discharged from the hospital. No adverse reactions were noted. One patient, whose wife was in the habit of using a contraceptive containing quinine, was patch-tested against quinine hydrochloride with negative results.

Summary and Conclusions

1. The course of nonspecific urethritis was studied in 136 British soldiers. The usual incubation period was 4 to 21 days.
2. The treatment schedules were various. Sulfanilamide and other sulfonamide drugs were used alone or in combination with irrigations. Irrigations only and calcium mandelate by mouth were given to some patients. No antibiotics were employed in this series.
3. Sulfanilamide proved a satisfactory drug, and the results were enhanced if irrigations and/or fever were combined. The results of combined therapy were superior to those of sulfonamides alone, irrigations alone, or of calcium mandelate alone, by mouth.
4. Cystoscopy of 57 patients revealed nothing of importance, and the passage of the instrument did not aggravate the disease.
5. Injections into the urethra of citrated whole blood taken from the patients themselves or from other persons failed to provoke a discharge in 11 recently cured persons.

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Penicillin in the Abortive Treatment of Syphilis[1]

Frederick Plotke, M. D., M. P. H.;[2] Henry Eisenberg, M. D.;[3] Amelia H. Baker, M. A.; and M. E. Laughlin, M. S., Statistician

It is obvious that an effective method for preventing syphilis in persons known to have been exposed would be of great value in the control of this disease. Therefore, an investigation of the abortion of syphilis has been carried on in one of the venereal disease clinics of the Chicago Health Department in order to try to determine whether or not the incidence of subsequent syphilis in a group of contacts of patients having infectious syphilis treated with 600,000 units of penicillin in peanut oil and beeswax (Romansky formula) would show any significant difference from a control group of untreated contacts. This investigation covered a period of 1 year, August 25, 1947, to August 24, 1948, and a 6-month period of follow-up on all cases. This study was initiated upon the request of Dr. Harry Eagle,[4] who was collaborating on a similar study with the Baltimore Department of Health.

Eagle, Magnuson, and Fleischman (*1*) had reported that relatively small doses of penicillin are required during the incubation period of syphilis in order to abort the development of the disease in rabbits.

Alexander and Schoch (*2*) have employed a "1-day abortive cure" treatment consisting of 900,000 units of calcium penicillin in oil and beeswax plus 120 mg. of bismuth plus 0.05 to 0.06 gm. arsenoxide given intravenously. Among 115 contacts who received this abortive treatment, 6 developed early syphilis. One hundred and thirty contacts were observed untreated, and 54 (41.5 percent) remained negative, while 75 (58.5 percent) developed syphilis.

Method of Study

All the sexual contacts named by patients diagnosed as having primary or secondary syphilis were considered potential study cases.

Sexual contacts were persons who were reported to have had intercourse with a syphilitic patient at any time during the 3-month period prior to the patient's onset of primary syphilis, or 5 months prior to the appearance of secondary symptoms.

When the full names and addresses of these contacts were known, telegrams were sent asking that they report immediately to the Director of the Epidemiology Section. If sufficient information to send telegrams was not available, field workers were assigned to bring in the contacts. When the contact reported in response to the telegram or as the result of field activity, he was interviewed by the Director of the Epidemiology Section or by a designated staff member.

Only persons meeting the following criteria were included in the study:

1. No syphilis diagnosis had previously been reported to the Health Department, and the contact did not admit ever having had such a diagnosis.
2. No penicillin had been given for any reason subsequent to the exposure date.
3. Exposure date did not exceed 3 months.

Those meeting these criteria were divided into control and treatment groups. In order to avoid any "discretionary" selection and also in order to give the laboratory time to do immediate serologic examinations, a time schedule was used in the assignment of the cases to these groups: from 9:00 a. m. to 2:30 p. m., the first of each three contacts reporting were designated as control cases, the next two as treatment cases, and so on until 2: 30 p. m. From 2: 30 p. m. until the closing of the clinic the contacts reporting were placed in the control group. A check was made once a week by the Epidemiology Section to determine the number of cases in each group. If either group was out of balance, all contacts reporting between 9: 00 a. m. and 2: 30 p. m. were placed in the smaller group until a balance was secured.

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[1] From the Venereal Disease Control Program, Chicago Board of Health, in cooperation with the U. S. Public Health Service. Under the direction of Herman N. Bundesen, Senior Surgeon (R) (Inactive), U. S. Public Health Service; President, Chicago Board of Health.

[2] Venereal Disease Control Officer, Chicago Board of Health.

[3] Senior Surgeon (R), U. S. Public Health Service.

[4] Then Senior Surgeon of the U. S. Public Health Service, Medical Officer in Charge, Laboratory of Experimental Therapeutics, Johns Hopkins School of Hygiene, Baltimore.

After a contact was interviewed, a complete diagnostic examination was made. Blood specimens from those persons with no history or clinical evidence of syphilis were sent immediately to the laboratory. After the existence of syphilis had been ruled out by serologic examinations, 600,000 units of penicillin in peanut oil and beeswax were administered in a single dose to those in the treatment group. If the contact in either group was found to have syphilis at the time of the first examination, the case was dropped from the study.

Contacts in both groups were instructed by the clinic epidemiologist to return for observation every 2 weeks for 3 months and once a month for the next 3 months, for a total of 6 months from the date of the first examination. During each clinic visit, a blood specimen was drawn for serologic examination, and a thorough physical examination was made for evidence of syphilis.

Any contact in the control group who had gonorrhea upon his first or subsequent visits was treated with sulfathiazole. If he was in the treatment group and had gonorrhea at the time of his first visit, the penicillin eliminated any evidence of gonorrhea. If he had gonorrhea upon subsequent visits, he was treated with sulfathiazole.

Results

Of the 1,069 contacts who reported, 927 cases were excluded from the study, mainly for the following reasons (table 1):

1. Penicillin had been given after the date of exposure.

Table 1.—*Contacts of patients diagnosed as having primary or secondary syphilis, by study group or reason for deletion from study and by disposition*

	Total number of contacts	Disposition						
		Not infected	Placed under treatment	Already under treatment	Cannot locate	Moved out of jurisdiction	Other	Case still open
Total cases	1, 069	372	300	95	177	82	39	4
Total cases accepted for study	142	105	18	--	---	10	7	2
Control group	65	39	15	--	---	5	4	2
Treatment group	77	66	3	--	---	5	3	--
Total cases not accepted for study	927	267	282	95	177	72	32	2
Reason for deletion:								
Penicillin for gc since exposure	26	17	7	--	---	1	1	--
Penicillin for other reason since exposure	7	5	2	--	---	--	--	--
Previous treatment for syphilis	136	20	64	45	---	--	7	--
Wished to transfer to private physician	34	23	10	--	---	--	1	--
Already under observation or treatment for syphilis	117	23	54	39	---	--	1	--
Exposure date over 3 months	95	75	13	4	---	1	1	1
Miscellaneous	86	40	29	3	---	9	5	--
Positive serology or symptoms on first examination	74	8	62	--	---	1	3	--
Reported diagnosis in error	14	9	--	--	---	2	3	--
Failed to respond to telegram: sent in by worker without interview for study	105	47	41	4	---	2	10	1
Unable to locate or found to live out of jurisdiction	233	--	--	--	177	56	--	--

Table 2.—*Contacts of patients diagnosed as having primary or secondary syphilis, by age, race, and sex*

Race and sex of contact	Total number of contacts	Age of contact					
		Under 20	20–29	30–39	40–49	50 and over	Unknown
Total cases	[1] 1,069	130	657	168	45	10	[1] 59
Male	570	25	354	113	32	10	36
Female	492	105	303	55	13	--	16
White and unknown	[1] 131	8	52	27	9	2	[1] 33
Male	66	1	24	18	6	2	15
Female	58	7	28	9	3	--	11
Negro and other	938	122	605	141	36	8	26
Male	504	24	330	95	26	8	21
Female	434	98	275	46	10	--	5
Total cases accepted for study	142	17	94	24	6	1	--
Male	71	3	50	14	3	1	--
Female	71	14	44	10	3	--	--
White and unknown	13	1	6	4	2	--	--
Male	7	--	4	2	1	--	--
Female	6	1	2	2	1	--	--
Negro and other	129	16	88	20	4	1	--
Male	64	3	46	12	2	1	--
Female	65	13	42	8	2	--	--
Total cases not accepted for study	[1] 927	113	563	144	39	9	[1] 59
Male	499	22	304	99	29	9	36
Female	421	91	259	45	10	--	16
White and unknown	[1] 118	7	46	23	7	2	[1] 33
Male	59	1	20	16	5	2	15
Female	52	6	26	7	2	--	11
Negro and other	809	106	517	121	32	7	26
Male	440	21	284	83	24	7	21
Female	369	85	233	38	8	--	5

[1] 7 cases included with sex not specified.

2. There had been previous treatment for syphilis.
3. The exposure date was over 3 months old.
4. There were positive findings on the first examination.

The remainder (142 cases) were accepted for the study. There were 77 cases in the treatment group and 65 in the control group.

It is significant in relation to the success of this study that a median of 6 days elapsed between the date the informant was interviewed and the date the contact reported and was examined.

Of the 1,069 contacts who reported, 233 could not be located at the end of the year's observation or had moved out of the jurisdiction. Of the remaining 836 contacts who were seen at least once, 395 were either placed under treatment or were found to be already under treatment. Therefore, 47.2 percent of the total group examined for syphilis were found to be infected.

Of the 142 cases accepted in the study, 71 were males and 71 were females; 13 were white and 129 were colored (table 2).

Table 3.—*Contacts of patients diagnosed as having primary or secondary syphilis, by study group and by type of contact*

	Total number of contacts	Contact of patient having—	
		Primary syphilis	Secondary syphilis
Total cases	[1] 1,069	296	773
Total cases accepted for study	142	50	92
Control group	65	21	44
Treatment group	77	29	48
Total cases not accepted for study	[1] 927	246	681

[1] Includes 14 cases diagnosed in error.

The median age of all cases examined was 26.2 years. Of the male cases, the median age was 27.4; of the female cases, 24.7; of the whites and race unknown, 32.6; and of Negroes and others, 25.8. If we compare those accepted in the study with the total number of contacts of patients having primary or secondary syphilis for the same period, we find no significant difference in age, sex, or color.

Of the control group of 65 cases, 21 were contacts of patients having primary syphilis and 44 were contacts of those having secondary syphilis (table 3). Of the 77 cases in the treatment group, 29 were contacts of patients having primary syphilis and 48 of those having secondary syphilis. In other words, almost twice as many cases were exposed to persons diagnosed as having secondary syphilis as to those diagnosed as having primary syphilis.

Of the 18 patients who developed syphilis and were placed under treatment (15 from the control group and 3 from the treatment group), all 3 in the treatment

Table 4.—*Contacts of patients diagnosed as having primary or secondary syphilis, by study group or reason for deletion from study and by diagnosis of infected cases*

	Placed under treatment					
	Total	Primary	Secondary	Early latent	Other late	Congenital
Total cases	300	45	94	100	57	4
Total cases accepted for study	18	8	9	1	--	--
Control group	15	5	9	1	--	--
Treatment group	3	3	--	--	--	--
Total cases not accepted for study	282	37	85	99	57	4
Reason for deletion:						
Penicillin for gc since exposure	7	5	1	--	1	--
Penicillin for other reason since exposure	2	--	1	1	--	--
Previous treatment for syphilis	64	5	13	27	17	2
Wished to transfer to private physician	10	1	3	--	6	--
Already under observation or treatment for syphilis	54	7	21	10	16	--
Exposure date over 3 months	13	--	2	10	--	1
Miscellaneous	29	6	12	7	4	--
Positive serology or symptoms on first examination	62	7	22	29	4	--
Reported diagnosis in error	--	--	--	--	--	--
Failed to respond to telegram: sent in by worker without interview for study	41	6	10	15	9	1

	Already under treatment					
	Total	Primary	Secondary	Early latent	Other late	Congenital
Total cases	95	16	38	24	14	3
Total cases accepted for study	--	--	--	--	--	--
Control group	--	--	--	--	--	--
Treatment group	--	--	--	--	--	--
Total cases not accepted for study	95	16	38	24	14	3
Reason for deletion:						
Penicillin for gc since exposure	--	--	--	--	--	--
Penicillin for other reason since exposure	--	--	--	--	--	--
Previous treatment for syphilis	45	10	17	15	3	--
Wished to transfer to private physician	--	--	--	--	--	--
Already under observation or treatment for syphilis	39	5	18	8	7	1
Exposure date over 3 months	4	1	2	--	--	1
Miscellaneous	3	--	--	--	2	1
Positive serology or symptoms on first examination	--	--	--	--	--	--
Reported diagnosis in error	--	--	--	--	--	--
Failed to respond to telegram: sent in by worker without interview for study	4	--	1	1	2	--

group developed primary syphilis, 5 in the control group were diagnosed as having primary syphilis, 9 as having secondary syphilis, and 1 as having early latent syphilis (table 4). The patient diagnosed as having early latent syphilis never showed signs or symptoms of having primary or secondary syphilis.

In both the control and treatment groups, we may assume that there were possible reexposures. Two of the three failures in the treatment group admitted reexposure. In the third case, no reexposure was admitted within the possible incubation period. The control group was not similarly investigated for reexposure.

The 15 patients in the control group who developed syphilis had a cumulative infection rate of 25.45 percent, and the 3 patients in the treatment group had a rate of 4.35 percent (table 5). This difference is statistically significant.

In the control group a median number of 66 days elapsed between the date of the last exposure to the informant and the date the first symptoms of syphilis were observed by the examining physician. The approximate period in the treatment group was almost twice as long. Those in the control group who developed syphilis showed evidence long before those in the treatment group. The same applies to the number of days between the date of the last exposure to the informant and the date of the last negative blood test before symptoms of syphilis appeared in the contacts. Here the median of the control group was 46 days and almost twice that time in the treatment group.

Thirty-eight days after the last day of exposure, the first case in the control group had positive findings upon examination. In no case did the positive findings develop later than 146 days after exposure. The comparable time in the treatment group (from 108 to 161 days) was, on the average, almost twice as long. This delay in the development of positive findings in the treatment group may be accounted for by the penicillin given.

It is of interest to compare the failure rate of the treatment group found by Alexander and Schoch and that found in our study. The failure rate in this study is not significantly different from that reported by Alexander and Schoch, though there is quite a difference in the amount of treatment given in the two studies.

Table 5.—*Contacts of patients diagnosed as having primary or secondary syphilis, by cumulative infection rate of contacts accepted in study*

Period of observation (in days)	Cumulative infection rate of contacts in—	
	Control group	Treatment group
1–29		
30–59	4.62	
60–89	19.95	
90–119	23.59	2.90
120–149	25.45	2.90
150–179	25.45	4.35
180 and over	25.45	4.35

Conclusions

When the exposure date was not in excess of 3 months, only about 4 percent of the treated contacts developed syphilis, while in the untreated or control groups about 25 percent contracted syphilis. Therefore, if contacts of patients having primary or secondary syphilis are found to be negative upon first examination, consideration should be given to treating them prophylactically. Such contacts should be given physical and serologic examinations monthly for 6 months.

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The Baffling Case of Baby T.[1]

E. Walter Shervington, M. D., Cornelia M. Phillips, R. N., and N. A. Nelson, M. D.

On May 19, 1948, G. T., a single female, 17 years of age, was admitted to the Baltimore City Health Department venereal disease clinic at the Druid Health Center because she had a positive serologic test for syphilis (Eagle flocculation), with a titer of 2 units; she was a little more than 4 months pregnant. A repeat test on May 26 was positive, titer 1.5. There was no history of syphilis, and there were no clinical signs of the disease. A diagnosis of early latent syphilis was made and the patient was referred to the Baltimore Rapid Treatment Center, where she received 4,800,000 units of sodium penicillin G in 14 days, from May 26 to June 10, on a 3-hour schedule around the clock.

Subsequent to this treatment she was observed at the Druid Health Center clinic once a month except in October 1948, when she delivered. The highest posttreatment titer was 3 units on November 15, 1948. The test was negative on December 29, 1948, and on January 21, 1949, since when it has fluctuated from doubtful to a titer of 1.5, to negative, and finally to a titer of 1 on May 9, 1949. She had a culture-positive gonococcic infection on February 4, 1949, the source of which could not be determined, as she denied any sexual contacts. For this she received 75,000 units of procaine penicillin in oil with 2 percent aluminum monostearate on February 11, 1949, with good results.

The alleged father of the infant, O. D., 21 years of age, married but separated from his wife, was first examined on May 27, 1948, as a contact of G. T., the original patient. There was no history of syphilis, and he stated that a test for syphilis, made on his discharge from the Navy in June 1946, was negative. The only evidence of infection with syphilis was a positive serologic test, titer 128. A repeat test on June 17 had a titer of 24. This man left Baltimore shortly thereafter and could not be located. He did not return to the city until after the birth of the baby and was not seen in the clinic until February 9, 1949. At that time he denied having had any lesions, and he had had no treatment for his syphilis. A serologic test was positive, titer 16.

The infant, O. T., was born at term, apparently healthy, on October 1, 1948, in Baltimore City Hospitals. A cord blood test was negative. On November 15, 1948, when the infant was 6 weeks of age, a serologic test was negative. On January 10, 1949, at the age of 3 months, its serologic test was positive, titer 256 plus.[2] On January 21 it was again positive, titer 256 plus,[2] and a zone reaction was noted. Axillary, inguinal, and epitrochlear glands were palpable, but there were no other clinical signs of syphilis, and the infant appeared healthy.

On February 7, 1949, the infant was admitted to the pediatric service at Baltimore City Hospitals, where X-ray examination of the skeleton revealed a generalized periostitis of long bones consistent with the diagnosis of congenital syphilis. A blood specimen was positive (Eagle flocculation, titer 256; Kahn flocculation, positive; cardiolipin flocculation, titer 128; Wassermann complement fixation, positive).

A diagnosis of congenital syphilis was made and the infant was given 640,000 units of sodium penicillin G at the rate of 8,000 units every 3 hours for 10 days. Its temperature rose to 101° F. after treatment was begun, but subsided, and the "entire hospital course was smooth." It was discharged in good condition on February 20, 1949. A serologic test for syphilis was positive on March 21, titer 256 plus, but on May 9 the titer had dropped to 24.

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[1] From the Bureaus of Venereal Diseases and of Public Health Nursing, Baltimore City Health Department.

[2] Not titered beyond this dilution.

There seems to be no doubt that this infant had syphilis. Since its serologic tests were negative at birth and at 6 weeks of age, it must have been infected very late in the prenatal period or else subsequent to birth.

In view of the mother's treatment, given in the fifth month of pregnancy, and the complete absence of any evidence of reinfection or relapse, it seemed impossible that the infant could have acquired its infection from its mother. The probability had to be considered that it had been infected after birth by contact with some other infected person.

As already noted, the alleged father had returned to Baltimore and was reexamined on February 9, 1949, but there was then no indication of openly infectious disease and no history of open lesions. He had seen the baby for a short time on only two or three occasions. A 19-year-old foster brother of his, R. M., living in the same household, was examined, and his serologic test was positive, titer 1.5, on February 11, 1949. He had a clear history of congenital syphilis, verified by the Johns Hopkins Hospital, for which he had received adequate treatment early in 1936 at the age of nearly 5 years. There was neither history nor evidence of a recent reinfection.

In the infant's household, besides its mother, there were 13 persons: a grandmother, 3 uncles, 3 aunts, and 6 cousins. All of these were examined repeatedly. Twelve of them had negative serologic tests for syphilis, and none of the 13 had, or could recall, any recent lesions. The grandmother's serologic test had a titer of 1 on February 4, 1949, at which level it remained through 4 tests at weekly intervals to March 7. No history of infection with syphilis could be obtained, and there was no clinical evidence of infection. It was concluded that she had late latent syphilis or a biologically false-positive test. It did not seem possible that she could have infected the baby.

Having arrived at no solution of the problem through this extensive epidemiologic study, the mother of the infant was again questioned as to her associates. She admitted, finally, that she had acquired a new "boy friend" while under treatment at the Rapid Treatment Center in May 1948. He was L. A., single, and 22 years of age.

L. A. had been admitted to the Druid Health Center clinic on May 27, 1948, with darkfield-positive primary syphilis, as the contact of a female patient with secondary syphilis. He was admitted to the Rapid Treatment Center on May 28, 1948, where he was treated with a combination of penicillin, bacitracin, and mapharsen in a special study of bacitracin in the therapy of syphilis. While at the Rapid Treatment Center he had become friendly with G. T., who was admitted on May 26, and this friendship was continued after they had been discharged from the hospital on June 7 and 10, respectively.

L. A. failed to report to the Druid Health Center for posttreatment observation, as directed, on July 2, 1948. It was reported to the public health nurse who visited his home that he had gone to California, address unknown. However, he returned to the clinic on September 9, 1948, and stated that he had been in jail for 60 days. On that date he presented a darkfield-positive lesion on the shaft of his penis, and there were several small, moist lesions under the prepuce (the original primary lesion had been on the frenum). His serologic test for syphilis was positive, titer 3 units. He stated that the current lesions had appeared in July, but he had not called them to the attention of the jail physician.

A diagnosis of secondary syphilis was made (relapse or reinfection?) and he was readmitted to the Rapid Treatment Center on September 11, 1948, where he received 4,800,000 units of sodium penicillin G. On December 6, his serologic test was positive, titer 12. He then spent another 2 months in jail and was lost to observation, but on March 22, 1949, his test was negative and his lesions healed. On April 19, 1949, he was named as a contact of still another female patient with primary syphilis. His observation following this exposure has not yet been completed.

Both L. A. and G. T. admitted their friendship but repeatedly denied sexual intercourse. There was ample opportunity for contact, however, between August 31 and September 11, 1948, after L. A. had left the jail and before he was readmitted to the Rapid Treatment Center and while he had infectious, darkfield-positive genital lesions, and their denials of contact could be given little weight. On the other hand, G. T. had shown no signs of reinfection or relapse at any time.

She was questioned carefully again and it was finally learned that she had returned to Baltimore City Hospitals 16 days postpartum on October 17, 1948, because of "female trouble." Her hospital record for this admission disclosed a diagnosis of "endometritis, mild," and she was given 3,000,000 units of penicillin. Her serologic test on this admission was positive but, unfortunately, had not been titered.

It now seems probable that G. T. was reinfected at some time just prior to delivery on October 1, 1948, and that she infected her baby. There is the possibility, of course, that she had a relapse of her own infection at that time, although this seems remote, since her sero-

Table 1.—***Chronologic record of the syphilis status of the three principal patients***

Date	G. T., mother of O. T.	O. T. (infant)	L. A., contact (?) of G. T.
1948			
May 19	STS positive, titer 2.		
26	Admitted to Rapid Treatment Center and treated. STS positive, titer 1.5.		
27			Primary syphilis, darkfield positive; STS positive, titer 3.
28	*G. T. and L. A. become friendly at Rapid Treatment Center.*		Admitted to Rapid Treatment Center and treated.
June 7			Discharged from Rapid Treatment Center.
10	Discharged from Rapid Treatment Center.		
July 2			In jail, July 2 to August 31.
9	STS positive, titer 1.		*New lesions appear in July. No medical care.*
Aug. 13	STS positive, titer 1.5.		
31			Discharged from jail.
Sept. 9	*Exposed to infection by L. A. (?).*		*Secondary syphilis, darkfield positive; STS positive, titer 3.*
11			Readmitted to Rapid Treatment Center and treated.
17	STS positive, titer 1.		
Oct. 1	*Delivered at Baltimore City Hospitals.*	*Born: cord blood negative.*	
17	*Readmitted to Baltimore City Hospitals. Endometritis. 3,000,000 units of penicillin.* STS positive, not titered.		
Nov. 15	STS positive, titer 3	*STS negative (age, 6 weeks).*	
Dec. 6			STS positive, titer 12.
29	STS negative.		
1949			
Jan. 10		*STS positive, titer 256 plus (age, 3 months).*	
21	STS negative	STS positive, titer 256 plus.	
Feb. 7		Admitted to Baltimore City Hospitals.	
21	STS doubtful.		
Mar. 8	STS positive, titer 1.5.		
15	STS negative.		
21		STS positive, titer 256 plus.	
22			STS negative.
Apr. 11	STS positive, titer 1.5.		
May 9	STS positive, titer 1	STS positive, titer 24.	

logic test on September 17, only 13 days before the birth of the baby, had a titer of 1. She was then treated, less than 3 weeks after the baby was born, with sufficient penicillin to cure the reinfection before it was detected, clinically or serologically. The titer of 3 on November 15 may reflect this reinfection, although it could very easily have been due to nothing more than laboratory variation.

The chronologic record of the syphilis status of the three principal patients is presented in table 1.

Summary

1. An infant, apparently healthy at birth and at 6 weeks of age, had syphilis at the age of 3 months.

2. The infant's mother had been treated for syphilis with penicillin when a little more than 4 months pregnant and, up to the time of the detection of syphilis in the infant nearly 8 months later, had shown no serologic or clinical signs of treatment failure.

3. The infant's father, the latter's brother, and the 13 members of the infant's household were repeatedly examined without disclosure of any infection which might have been the postnatal source of the infant's infection.

4. It was eventually learned that the infant's mother had acquired a new "boy friend" who had infectious syphilis to which the mother might have been exposed within a month prior to the birth of the baby.

5. It was finally learned that she had been given 3,000,000 units of penicillin 3 weeks after the birth of the infant, for another condition, which may very well have cured an infection acquired just before the birth of the infant and have prevented its detection. This undetected infection appears to be the only possible source of the infant's infection.

CURRENT NOTES AND REPORTS

VD Radio Programs

Since July 1, 1948, 89 radio stations in 16 States, in cooperation with their local health authorities, have broadcast more than 3,000 programs and announcements in support of local syphilis case-finding campaigns. These 1,184 15-minute programs and 1,860 announcements have reached a conservatively estimated 25 million listeners.

Featured in these broadcasts was a series of 14 star-studded 15-minute electrical transcriptions; two special messages by Drew Pearson and Rev. Adam Clayton Powell; and a platter of varied-length spot announcements by outstanding personalities, prepared and produced by Columbia University, under the supervision of Erik Barnouw, in cooperation with the United States Public Health Service. The transcribed series received a special award in the "Personal and Social Problems' category at the Thirteenth Annual American Exhibition of Education by Radio in Columbus, Ohio.

Not included in the above list of broadcasts was much special programming which was developed by many individual stations as feature supplements to the transcribed series. Through these programs local audiences got the local story from local authorities and key personalities.

The encouragement given health authorities throughout the country by radio's willingness to attack the public problem of venereal disease has prompted these authorities to band together in an intensive, simultaneous public appeal campaign in over 300 communities in 28 States. Among the many public appeal materials being prepared are posters, pamphlets, movies, and a hard-hitting top talent series of music-drama transcriptions which will be made available by the Communication Materials Center of Columbia University Press to local health authorities for radio programming on all radio stations.

Virginia Offers VD Consultation Service

A new, free-of-charge Venereal Disease Consultation Service for patients with complicated "problem" cases of venereal disease was offered to physicians in Virginia starting May 1, 1949. This was announced by Dr. L. J. Roper, State Health Officer, in the Virginia Department of Health morbidity report for the week ended April 16, 1949.

The service, made available by the State Health Department and the Medical College of Virginia, may be used by the patients of any physician in the State who desires a complete evaluation, which will include a case history, a physical examination, serologic tests for syphilis, examination of the cerebrospinal fluid, and such additional laboratory examinations and special consultations as may be necessary. The patient will then be returned to the referring physician, who will be sent a complete report of the examinations, together with specific and detailed recommendations for future management.

While the service is free of charge, the patient must pay for hospitalization or treatment, as well as for transportation and living costs while being examined (1 to 2 days).

The service is available on an appointment basis, and request forms may be procured from county health departments and from the Venereal Disease Consultation Service of the Medical College of Virginia.

Navy Reports on VD Contact Investigation

The results of the contact information supplied by the Department of the Navy to the civilian health agency, investigated by them, and reported back to the Navy Bureau of Medicine and Surgery for use in its venereal disease control program were reported for the first quarter of 1948 in the January issue of *Statistics in Navy Medicine*. The data reported on represent approximately two-thirds of all the reports submitted to the health departments for this period. The reports that were not returned, according to the Navy, may cause a bias in the percentage results for specific localities.

Investigations of venereal disease contacts by civilian authorities in the continental United States were considerably more successful than those conducted in foreign areas. In the United States, out of 2,988 contact reports returned to the Navy, 17.8 percent resulted in the contact being located and put under treatment for the first time. In foreign areas, 2.9 percent of the reports returned resulted in location of an infected contact who was put under treatment for the first time. In both areas, however, the amount of information submitted on the great majority of the reports was considered inadequate by the health departments for efficient follow-up of the contacts.

In the continental United States, of

the 2,988 contact reports returned, 25.3 percent had, in the opinion of the health authorities, insufficient data to start the investigation; in 40.1 percent of all the cases the investigation was unsuccessful. In foreign areas, of 1,906 contact reports in the quarter, 72.2 percent were considered to have insufficient data to start investigation and an additional 13.9 percent resulted in unsuccessful investigations. Thus, 65.4 percent of the contact reports proved useless for locating contacts in the continental United States and 86.1 percent were unsuccessful in foreign areas.

The distribution by location, however, shows considerable variation among the specific localities as to the results of the investigations of contact reports returned by their respective health agencies, the percentage placed under treatment varying from 36.4 percent in 1 State to 0 in another. In the continental United States, 7 States and 1 district were listed as having more than 100 contacts each. These were California, the District of Columbia, Florida, Louisiana, New York, South Carolina, Virginia, and Washington. These 8 areas accounted for 81.0 percent of all the contact reports returned in the United States. The distribution of the strength of the Navy and Marine Corps in the United States is the primary factor responsible for this occurrence. California and Virginia combined sent in almost 50 percent of all the contact reports which were returned to the Navy for the entire continental United States. The two cities returning the greatest number of contact reports were San Diego, Calif., and Norfolk, Va., with 28.1 percent of the total number of contact reports for the continental United States.

For those exposures occurring in foreign areas, the Caribbean area and Central America returned 1,098 contact reports, or 57.6 percent of the total for foreign areas, while the Far East area returned another 27.1 percent. The foreign cities returning the greatest number of contact reports were Tijuana with 402 and Tsingtao with 383. These cities combined sent in 41.2 percent of all the contact reports returned by foreign areas.

CURRENT LITERATURE

Note: Abstracts of any article listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

Acta dermat.-venereol., Stockholm

Recherches sur l'action gonococcide du sérum humain. (The gonococcidal action of human serum.) Olaf Nørgaard. 29: 421–442, Fasc. 5, 1949.

Changes in the serum globulin content in the development of and the recovery from early syphilis. B. A. Verhagen. 29: 443–459, Fasc. 5, 1949.

Review of dermatology and venereology. Transactions of Swedish Dermatological Society for the year 1947. 29: 506–538, Fasc. 5, 1949.

Am. J. Clin. Path., Baltimore

A method for the quantitative measurement of complement-fixation. E. E. Ecker and C. W. Hiatt. 19: 141–151, Feb. 1949.

Specificity of cardiolipin antigens in tests for syphilis. Sara C. McDearman and James E. Cottrell. 19: 156–162, Feb. 1949.

Standard Kline test of cerebrospinal fluid for syphilis. Employing in cardiolipin-lecithin antigen. B. S. Kline and H. Susssenguth. 19: 274–277, Mar. 1949.

Universal serologic reaction with lipid antigen. I. In normal persons. Reuben L. Kahn. 19: 347–360, Apr. 1949.

Universal serologic reaction with lipid antigen. II. In animals. Reuben L. Kahn and Betty J. Baribeau. 19: 361–368, Apr. 1949.

Universal serologic reaction with lipid antigen. III. In syphilis. Reuben L. Kahn and Elizabeth B. McDermott. 19: 401–407, May 1949.

Am. J. M. Sc., Philadelphia

The effect of benzoic acid and caronamide on blood penicillin levels and on renal function. John F. Waldo, John M. Masson, Wan Ching Lu and Jeanne Tollstrup. 217: 563–568, May 1949.

Am. J. Med., New York

* Penicillin in oil and beeswax in the treatment of syphilis in clinic patients. Henry Eisenberg and Frederick Plotke. 6: 449–452, Apr. 1949.

Penicillin in oil and beeswax in the treatment of syphilis in clinic patients. Henry Eisenberg and Frederick Plotke. Am. J. Med., 6: 449–452, Apr. 1949.

A statistical report was made on the attendance from February 1947 to February 1948 at Chicago Health Department clinics of 1,000 syphilis patients treated on an ambulatory 10- or 15-day schedule basis with penicillin in oil and beeswax.

The largest group treated constituted late latent syphilis with 59.6 percent of all patients. The next largest group was neurosyphilis with 24.9 percent. There was no appreciable difference in the race and sex rate.

All patients were instructed to return daily for their prescribed treatment except on Saturdays and Sundays but they were permitted to lapse for 2 days between treatment days before the lapse was considered permanent. Patients who attended the clinic three or more times a week, completing 10 injections within 21 days, were considered to have completed their treatment satisfactorily. If a patient lapsed for more than 2 days between treatments, he was reinstituted on the prescribed treatment schedule.

The prescribed treatment was completed by 859 (85.9 percent) of the total 1,000 patients. Of the 767 patients on the 10-day schedule, 87.0 percent completed the course, and 82.4 percent of the 233 patients on the 15-day regimen completed the treatment.

Because of local or allergic manifestations, 28 patients discontinued or lapsed treatment. Intercurrent illnesses, either personal or within their families, caused

60 patients to fail to complete treatment. For unknown reasons, 125 patients disappeared from observation.

It is concluded that ambulatory treatment with penicillin in oil and beeswax is far superior, as regards clinic attendance, compared to the 30.0 percent attendance recorded for long-term chemotherapy.

AM. J. OBST. & GYNEC., ST. LOUIS

*The use of crystalline penicillin G in the treatment of syphilis in pregnancy. John B. Cross, John R. McCain and Albert Heyman. 57 : 461–465, Mar. 1949.

Primary and secondary spontaneous habitual abortion. [Syphilis.] Carl T. Javert, William F. Finn and Henricus J. Stander. 57 : 878–889, May 1949.

An analytical survey of multigravidas. [Syphilis.] James M. George and Howard A. Power. 57 : 972–979, May 1949.

The use of crystalline penicillin G in the treatment of syphilis in pregnancy. John B. Cross, John R. McCain and Albert Heyman. Am. J. Obst. & Gynec., 57 : 461–465, Mar. 1949.

A report is presented of the use of crystalline penicillin G in the treatment of 39 pregnant women with early syphilis. The diagnoses of these patients at the time of treatment were as follows: seropositive primary syphilis, 2; secondary syphilis, 25; recurrent syphilis, 2; early latent syphilis, 10. None of the patients had had treatment except the 2 with recurrent secondary manifestations. Thirty-six of the patients were Negro and 3 were white.

Each patient received a total dose of 4.8 million units of crystalline penicillin G, administered in doses of 80,000 units every 3 hours for 60 injections in 7½ days. Twenty patients were treated between the sixteenth and thirty-second weeks of pregnancy; 14, after the thirty-second week; while only 5 began their treatment before the sixteenth week. All patients have been followed for at least 4 months after delivery.

Six patients went into premature labor during penicillin therapy, and 2 of their children were born with congenital syphilis. One patient developed a serologic relapse prior to parturition and delivered a syphilitic child. There were 4 infant deaths, 2 of which were probably caused by syphilis. The remaining 32 children are living and are nonsyphilitic.

Of the 39 patients treated for syphilis in pregnancy, 34 have obtained a satisfactory clinical and serologic response. Five patients (12.8 percent) have developed evidence of treatment failure following therapy. These patients were not retreated prior to delivery because the rise in quantitative titer did not become significant until parturition. Only 1 of their children showed evidence of syphilis, however.

The results of this study indicate that crystalline penicillin G is of considerable value in the prevention of congenital syphilis, even when given late in pregnancy. It has been estimated that approximately 95 percent of patients with early untreated syphilis detected late in pregnancy will have congenitally syphilitic children if no treatment is given. In this study only three living children had syphilis, and two of these were delivered before the therapy was completed. The two stillbirths in this study were probably the result of severe syphilitic infection which had produced such advanced tissue destruction that no form of therapy would have been successful. For this reason treatment with penicillin should be started early in pregnancy if possible. The abortion which occurred in the fifth month of pregnancy may have been caused by eclampsia. Another death, that of a child who died 3 days after delivery, was adequately explained at autopsy by the presence of extensive bronchopneumonia.

It is difficult to compare results in this study with those obtained with arsenical therapy, but there is no doubt that penicillin is more effective. The relapse rate in this series of patients is comparable to that generally obtained with penicillin in early syphilis after a similar period of follow-up observation.

ANN. INT. MED., LANCASTER

*The effect of caronamide on the blood concentration of penicillin following oral and intramuscular administration of penicillin. William W. Zeller, Mark H. Lepper, Jay A. Robinson, Harold L. Hirsh and Harry F. Dowling. 30: 398–407, Feb. 1949.

The effect of caronamide on the blood concentration of penicillin following oral and intramuscular administration of penicillin. William W. Zeller, Mark H. Lepper, Jay A. Robinson, Harold L. Hirsh and Harry F. Dowling. Ann. Int. Med., 30: 398–407, Feb. 1949.

A study was made at Gallinger Municipal Hospital of the effect of caronamide upon the serum penicillin concentrations in 106 patients who were receiving penicillin orally or parenterally. The patients selected showed no evidence of impaired renal function.

Following the administration of penicillin alone and then the same dose of penicillin plus caronamide, for at least 12 hours, the concentrations of penicillin in the blood were determined. Each patient served as his own control. The "caronamide bloods" were drawn 24 hours after the "control bloods" at the corresponding hourly intervals in the same patients. A modification of the Rammelkamp method was used to assay penicillin concentrations in the serums.

A statistical evaluation of the differences between the mean caronamide levels and the mean control penicillin levels is presented in detail. For the purpose of analysis the patients were divided into groups: Those who received 30,000 units of penicillin intramuscularly every 3 hours ("selected intramuscular series"), those who received 100,000 units orally every 4 hours ("selected oral series"), and both groups considered together ("total selected series"). Varying doses of oral caronamide were administered to all of the patients.

It was found that caronamide increased the height of the serum penicillin concentrations for at least one of the hourly intervals tested in 92 percent of the patients. Regardless of the route of administration of penicillin, the average increase in serum penicillin concentrations attained with the use of penicillin plus caronamide was four times as great as that obtained with the use of penicillin alone.

There was little evidence of acute toxicity to caronamide observed. The group of patients studied was not large enough to determine chronic toxicity.

Caronamide was used to best advantage clinically with the oral administration of penicillin. It is suggested that when penicillin is administered parenterally, it may be more economical to increase the dose of penicillin rather than give caronamide if higher and more sustained concentrations of penicillin are desired. The recommended dose of caronamide is 4 gm. administered every 4 hours.

The authors state that since experience with the use of caronamide has been brief, many problems concerning its use with penicillin remain for future investigation.

ARCH. DERMAT. & SYPH., CHICAGO

Treatment of early syphilis with sodium penicillin. A preliminary report with a comparison of results with 4,800,000 units, administered in seven and a half days, with smaller dosages. James Q. Blackwood, Virgil Scott and E. Gurney Clark. 57: 1028–1041, June 1948.

ARCH. INT. MED., CHICAGO

*Prognosis in late latent syphilis. Henrik L. Blum and Charles W. Barnett. 82: 393–409, Oct. 1948.

Prognosis in late latent syphilis. Henrik L. Blum and Charles W. Barnett. Arch. Int. Med., 82: 393–409, Oct. 1948.

The prognosis for 2,566 patients at Stanford Clinic with late latent syphilis was studied and analyzed in relation to treatment: 1,682 patients were followed for 1 year; 628, for 5 years; and 316, for 9 years or more.

This study was entirely clinical, and a patient who remained in the latent stage was classified as unchanged regardless of his serologic status. Progression was used to indicate that there had appeared definite or probable clinical evidence of syphilis during the period that the patient had been under observation in the clinic. Central nervous system progression, cardiovascular progression, gummatous progression, and probable progression are described.

The analysis of the prognosis in latent syphilis and of the effect of treatment on it was based entirely on the frequency of clinical progression per patient year of observation. In order to avoid small figures, the incidence of relapse was multiplied by 100 and was given in terms of patient centuries of observation, designated at "per century" for the sake of brevity. According to the authors, this method of study permitted the inclusion of a large number of patients observed for short periods who would otherwise have to be eliminated, which resulted in a great augmentation of the total data and provided a more representative sample of late latency. Also, it did not require the exclusion of progressions because they happened to have been noted within an arbitrary minimum period. Observation periods were computed to the nearest year, and the shortest time considered was just over 6 months.

Incidence of progressions per century of observation according to duration of observation; frequency of progressions in relation to race, sex, age, previous treatment; and relation to treatment at the clinic are shown in table form.

According to the authors, the century of observation method gives a clearer conception of prognosis and of the influence of treatment than does the per capita method because it introduces the factor of time and thus furnishes some notion as to when a progression might be expected rather than a crude estimate of the total probability of progression, provided the patient lives long enough to have one. In a group of patients who had no, or insufficient, treatment prior to observation, there was approximately one advance per century of observation. For a patient of 45 years who has a life expectancy of about 25 years, the chances that trouble will eventually develop would be 1 in 4. With adequate treatment, the incidence of progression is reduced to once in 5 centuries, and the chance of eventual progression in the patient of 45 is only about 1 in 20.

The prognosis in late latent syphilis appears to be improved by treatment at any time, and there seems to be steady improvement with increasing amounts of therapy. The conventional course treatment of 20 injections of arsenic and 20 injections of bismuth is only about one-half of a truly adequate regimen.

It is suggested that by the use of the proposed method of analysis it should be possible to determine the value of penicillin in latent syphilis in a few years, if a large group of patients were treated, rather than in the 10 to 25 years previously thought necessary for such a study.

Arch. Ophth., Chicago

*Treatment of ocular syphilis with penicillin. Curtis D. Benton, Jr. and Albert Heyman. 40: 302–310, Sept. 1948.

Treatment of ocular syphilis with penicillin. Curtis D. Benton, Jr. and Albert Heyman. Arch. Ophth., 40: 302–310, Sept. 1948.

The results of penicillin treatment of 39 patients with various manifestations of syphilis of the eye are reported.

Of 15 patients treated for acute active interstitial keratitis, 3 had had previous episodes of keratitis, while 12 were affected for the first time. All were thought to have congenital syphilis. One patient had received previous treatment for syphilis with 2,400,000 units of penicillin 6 months before the onset of interstitial keratitis, while 2 other patients had received a total of 10 and 30 injections of arsenical and bismuth preparations several years previously. The 3 patients treated for recurrence of keratitis had received inadequate arsenical and bismuth therapy for their initial keratitis. Treatment in 5 of the 7 adults consisted of 4,000,000 units of commercial penicillin given in doses of 50,000 units intramuscularly every 3 hours for 10 days. One patient received a total of 2,000,000 units, while the seventh received 3,000,000 units. The children were given an initial dose of 50,000 units of penicillin per kilogram of body weight which was subsequently increased to 100,000 units. Six of the patients who showed no response to penicillin at the completion of treatment were given fever therapy with typhoid vaccine. A total of 20 eyes were treated for an initial infection and 4 eyes for recurrent infection. Penicillin produced little or no immediate response, but clearing of the opacity and subsidence of the inflammation occurred in most patients 3 to 5 months after therapy. Sixteen (80 percent) of the 20 eyes treated showed good to excellent vision after a follow-up of from 8 months to 2 years.

Six patients with secondary syphilis and iritis were treated with penicillin alone, with a dosage varying from 2,400,000 to 4,000,000 units given in equally divided amounts intramuscularly every 3 hours for 7 to 10 days. Atropine was used locally. All six patients improved rapidly and obtained a final visual acuity of 20/20 in each eye. In addition, three patients with iritis associated with late syphilis were treated, but only one responded to the treatment.

Three patients with acute syphilitic meningitis and bilateral papilledema were treated with 4,000,000 units of sodium penicillin intramuscularly, in equally divided doses every 3 hours for 10 days. All showed satisfactory subsidence of the papilledema and relief of the meningeal symptoms.

Of 12 patients with progressively decreasing vision caused by syphilitic primary atrophy of the optic nerve, 8 had received previous treatment for syphilis consisting of inadequate amounts of heavy metals many years before the development of the optic nerve atrophy. One patient had received 54 hours of fever therapy 1 year prior to the present admission, but had continued to show progression of the optic nerve. Another had received 1,200,000 units of penicillin 2 years previously. Penicillin was given intramuscularly in doses of approximately 50,000 units every 3 hours for 7 to 16 days, with a total dosage of 2,400,000 to 6,000,000 units. Four of the patients received fever therapy in addition to penicillin. Six of the 12 patients showed progression of their optic nerve atrophy 6 months to 2 years after treatment. Of the 8 patients treated with penicillin alone, 4 showed apparent arrest of the process. In 6 of the patients, the condition progressed to practical blindness. Regardless of the response of the vision, all the patients showed a satisfactory or improved condition of the spinal fluid 6 months to a year after penicillin treatment.

Penicillin appears to be of value in the treatment of ocular manifestations of syphilis and should be used in combination with fever therapy for atrophy of the optic nerve.

Arizona Med., Phoenix

The American College of Physicians. [Syphilis.] 6 : 43, 45, Apr. 1949.

Bol. Ofic. san. panam., Washington

Treatment as a factor in the control of venereal diseases. Robert D. Wright and Francis P. Nicholson. 28 : 462–468, May 1949.

Brit. M. J., London

Treatment of gonococcal vulvovaginitis. No. 4607 : 719, Apr. 23, 1949.

Extrathoracic pain in cardiovascular disease. J. L. Lovibond. No. 4610 : 833–837, May 14, 1949.

The use of procaine penicillin in children. J. L. Emery, S. M. Stewart and D. G. Stone. No. 4610 : 845–846, May 14, 1949.

California Med., San Francisco

The experimental and clinical use of polymyxin, chloromycetin, and aureomycin. P. H. Long, E. B. Schoenbach, E. A. Bliss, M. S. Bryer and C. A. Chandler. 70 : 157–166, Mar. 1949.

Meningovascular myelitis in early syphilis. Ernest K. Stratton. Case reports. 70 : 209–210, Mar. 1949.

Cincinnati J. Med., Cincinnati

The importance of accurate venereal disease reporting. Carl A. Wilzbach and Catherine E. Ludlow. Public Health Section. 30 : 293–294, May 1949.

The so-called quick cures for V. D. Roy E. Dickerson. Public Health Section. 30 : 353, June 1949.

Clin. Med., Waukegan

Blood test. Medical News. 56 : A–12, May 1949.

Connecticut Health Bull., Hartford

Social hygiene guidance. A report of three years' progress. [V. D.] William F. Benedict. 63 : 187–192, July 1949.

Epidemiol. and Vital Stat. Rep., Geneva

Syphilis and gonorrhoea in Germany. Thorstein Guthe. 2 : 2–15, Jan. 1949.

INDIAN J. VEN. DIS., BOMBAY

Investigation on complement fixation reaction in gonorrhoea. A. N. Roy, J. Mukherjee and S. Sen. 15 : 16–19, Jan.–Mar. 1949.

Venereal diseases and the general practitioner. N. Anantha Rao. 15 : 19–22, Jan.–Mar. 1949.

INTERNAT. HEALTH BULL., GENEVA

Risks and drawbacks in the use of certain new drugs. Maurice Roch. 1 : 20–23, Jan.–Mar. 1949.

J. A. M. A., CHICAGO

Prophylaxis of ophthalmia neonatorum. Editorial. 140 : 410–411, May 28, 1949.

J. AM. M. WOMEN'S A., NASHVILLE

Recent advances in gynecology. With special emphasis on diagnosis and treatment of early cancer. [V. D.] Eloise Parsons. 4 : 145–150, Apr. 1949.

Dermatology and syphilology. 4 : 152–158, Apr. 1949.

J. AM. PHARM. A. (PRAC. PHARM. ED.) EASTON

Aureomycin. A new antibiotic for the treatment of bacterial, viral, and rickettsial diseases. 10 : 168–169, 180–181, Mar. 1949.

J. EXPER. MED., NEW YORK

*Immobilization of *Treponema pallidum* in vitro by antibody produced in syphilitic infection. Robert A. Nelson, Jr. and Manfred M. Mayer. 89 : 369–393, Apr. 1, 1949.

Immobilization of *Treponema pallidum* in vitro by antibody produced in syphilitic infection. Robert A. Nelson, Jr. and Manfred M. Mayer. J. Exper. Med., 89 : 369–393, Apr. 1, 1949.

The authors demonstrated the presence of antibody in serums from syphilitic animals and human beings which immobilized virulent *Treponema pallidum* in vitro. They present in detail their findings with regard to : (1) the immobilizing activity of the specific antibody acting in conjunction with complement and the immobilization of treponemes which when immobilized are noninfectious and presumably dead ; (2) the factors which affect the measurement of the immobilizing antibody in serums from animals and human beings in various stages of syphilitic infection ; (3) the occurrence of this antibody in serums from animals and human beings in various stages of syphilitic infection ; (4) the differentiation of the immobilizing antibody from the Wassermann antibody or reagin.

Normal and syphilitic serums of rabbits were tested with and without guinea pig complement for their immobilizing activity on *T. pallidum.* Neither serum pool exerted a significant deleterious effect on the motility of *T. pallidum* in the absence of guinea pig complement. A marked reduction in motility of the organisms was produced by the syphilis serum pool, but not by the normal serum pool in the presence of complement. The component of syphilis serum responsible for the immobilization was believed to be an antibody against *T. pallidum.* To verify this fact further the authors showed that heat inactivation or removal of complement by absorption with a specific precipitate rendered guinea pig serum incapable of immobilizing *T. pallidum* in conjunction with syphilitic rabbit serum.

The immobilizing effect increased with time and with serum concentration and was manifested rather slowly. The rate of antibody action increased with temperature. Immobilizing activity was exhibited only in the presence of complement and approached maximal intensity with a final guinea pig serum dilution of 1/10 to 1/20.

To prove that the effect of the antibody was treponemicidal, total counts and the percentages of motile organisms were made in three mixtures of treponemes, serum, and complement, incubated at 30° C. for 16 hours. In one test, rabbits were injected with a sample containing 4 percent motile organisms and two samples containing 78 and 80 percent motile organisms, respectively. Significant differences were observed in the incubation period for the development of the lesions and in the size of the lesions. Another test was performed with organisms exposed to complement plus serum ultrafiltrate (control) and another to complement plus syphilitic serum. All sites on the three rabbits inoculated with the control mixture (treponemes 90 percent motile) developed typical darkfield-positive lesions within 6 days. Only one of the sites inoculated with treponemes exposed to syphilis serum complement (0 percent motile) developed a darkfield-positive lesion. This indicated, according to the authors, that *T. pallidum* immobilized by antibody and complement were noninfectious and presumably dead.

A survey was made to determine the presence of immobilizing antibody in animal and human serums. Of 20 cases of human primary syphilis tested, 10 showed a marked immobilizing action, 3 exhibited weak activity, and 7 were without effect. A marked degree of immobilizing activity was exhibited in all serums from 20 cases of secondary syphilis. All the serums from syphilitic animals gave strongly positive reactions. Twenty serums examined from normal human beings were completely devoid of immobilizing activity, as were 16 of the 20 serums from patients with diseases other than syphilis. Inconclusive results in the other 4 were believed to be due to the penicillin in the serum. Seventeen of 20 normal serums of rabbits were completely negative and the other 3 exhibited weak activity.

From absorption experiments the authors concluded that immobilizing and reagin activities were due to separate antibodies and that reagin played no role in immunity. Furthermore, they believed that the immobilizing antibody killed *T. pallidum* and must therefore be responsible for the immune state.

J. FLORIDA M. A., JACKSONVILLE

Report of committee on venereal disease control. Jack A. McKenzie. Proceedings Seventy-Fifth Annual Meeting. 35: 771, June 1949.

J. IMMUNOL., BALTIMORE

The origin and nature of Wassermann antibody alias reagin. Bernard D. Davis. Letters to the Editors. 61: 373–374, Apr. 1949.

J. INFECT. DIS., CHICAGO

Cross immunity studies between virus strains in the psittacosis-lymphogranuloma venereum group. John C. Wagner, Orville J. Golub and Vivian W. Andrew. 84: 41–46, Jan.-Feb. 1949.

J. INVEST. DERMAT., BALTIMORE

Streptomycin therapy of chronic granuloma inguinale. M. Harriss Samitz, Peter N. Horvath, Primo P. Mori and Herman Beerman. Preliminary and Short Reports. 12: 85–93, Feb. 1949.

J. KANSAS M. SOC., TOPEKA

The use of penicillin in the ambulatory treatment of syphilis in pregnancy. Max S. Allen and Mahlon H. Delp. 50: 116–119, Mar. 1949.

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J. LAB. & CLIN. MED., ST. LOUIS

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J. M. A. ALABAMA, MONTGOMERY

Venereal disease control. [Alabama.] Transactions of 1949. 18: 375, June 1949.

J. MICHIGAN M. SOC., ST. PAUL

*Procaine penicillin with aluminum monostearate. Serum concentrations after oral and intramuscular administration. Jean M. Robinson. 48: 337–342, Mar. 1949.

Procaine penicillin with aluminum monostearate. Serum concentrations after oral and intramuscular administration. Jean M. Robinson. J. Michigan M. Soc., 48: 337–342, Mar. 1949.

This study was undertaken to determine the serum penicillin levels obtained using both the intramuscular and oral routes, and with different dosages of procaine penicillin. A total of 110 patients were used for the intramuscular studies; 40 patients were studied using oral preparations. The intramuscular preparation used was procaine penicillin G (small-particle size) suspended in peanut oil with 2 percent w/v aluminum monostearate, and crystalline penicillin G buffered and unbuffered was the oral preparation.

Observations were made on a number of patients who received the intramuscular preparations to study what effect muscular activity had upon the serum penicillin levels. In another group of patients a series of multiple injection studies was done to determine how high the serum penicillin concentration would rise; how well the high levels were maintained; and what side reactions, if any, would occur when the high levels were reached. Several dosage schedules which were followed are described.

To study the duration of therapeutic

serum penicillin levels obtained by the oral administration of penicillin preparations, buffered and unbuffered, single doses of 100,000 units of crystalline procaine penicillin G with 2 gr. (0.13 gm.) aluminum monostearate buffered with 4 gr. (0.26 gm.) $CaCO_3$ were given to 5 patients. Serum penicillin concentrations at 1, 2, 4, 8, 16, and 24 hours were compared with respect to duration of effective levels with those obtained using 100,000-unit doses of three other buffered crystalline preparations not containing aluminum monostearate. Further studies were done in 20 patients, using much greater amounts of oral crystalline penicillin G (500,000 and 1,000,000 units) buffered and unbuffered, to determine the concentration of penicillin obtained in the serum at 1, 2, 4, and 8 hours, and the duration of effective blood levels with the buffered products as compared to the unbuffered.

The results are presented in table form. A single injection of 1 cc. (300,000 units) of procaine penicillin (small particle size) suspended in peanut oil with 2 percent w/v aluminum monostearate was found to give therapeutic serum penicillin concentrations during the first hour after injection; it maintained therapeutic levels for 72 hours in 90 percent of cases and maintained therapeutic levels for 96 and 120 hours in 70 percent of the cases.

Serum levels ranging from 5 to 30 times the minimal level of 0.03 units/cc. for 24 and 12 hours, respectively, following the last injection were obtained by injections of 1 cc. of the intramuscular penicillin every 24 hours and every 12 hours for five successive days. Injection of 2 cc. (600,000 units) every 24 hours for five successive days gave serum levels 8 times the minimum therapeutic level at 1 hour after injection, and the serum levels were maintained at 0.03 units/cc. or higher for 24 hours after the last injection. Sensitivity reaction occurred in only 1 patient of the 24 who received multiple injections.

Oral crystalline procaine penicillin with 2 gr. (0.13 gm.) aluminum monostearate, buffered with 4 gr. (0.26 gm.) $CaCO_3$, given in single doses of 100,000 units, gave serum penicillin concentrations which were adequate but generally lower at 1, 2, and 4 hours, and higher at 8 hours than levels obtained by the use of three other oral buffered crystalline penicillin preparations. Much larger doses (500,000 and 1,000,000 units per tablet) of crystalline penicillin G, buffered and unbuffered, gave adequate serum penicillin concentrations for only 8 hours, and the serum levels of the buffered products were higher than those of the unbuffered.

J. NAT. M. A., NEW YORK

* Treatment of yaws in the Haitian peasant. Charles R. Rein. 41 : 60–65, Mar. 1949.

Modern management of prenatal syphilis and prevention of congenital syphilis. W. H. Johnson. 41 : 126–127, May 1949.

Treatment of yaws in the Haitian peasant. Charles R. Rein. J. Nat. M. A., 41: 60–65, Mar. 1949.

A study was made of 500 primary and secondary yaws patients in Haiti who were treated with penicillin. A preliminary report was published in 1946. This subsequent report presents a detailed evaluation of the results obtained in the entire group at the end of 12 months of observation.

The patients were divided into three groups: (1) Group A comprised 200 patients who were hospitalized and given 1.2 million Oxford units of sodium penicillin in aqueous solution over a 4-day period (30 intramuscular injections of 40,000 Oxford units every 3 hours day and night). All patients received the same dose regardless of age. (2) Group B comprised 151 patients who were treated on a 2-day ambulatory schedule with amorphous calcium penicillin in peanut oil and beeswax. Children 6 to 12 years of age received 600,000 Oxford units; those 17 years and older were given 1.2 million Oxford units. The penicillin was given intramuscularly in divided doses 24 hours apart. (3) Group C comprised 149 patients who were treated on a 1-day ambulatory schedule with the same amorphous calcium penicillin in peanut oil and beeswax. The same dose modification according to age was employed as in group B, but the doses were administered 10 to 12 hours apart.

The clinical response obtained with penicillin therapy was consistently and invariably good in all of the patients. The rapid and complete healing of generalized, large frambesia lesions was dramatic. Approximately 93 percent of the patients showed satisfactory serologic progress, but only 15.8 percent had attained seronegativity at the end of the observation period.

From this study it is concluded that the amount of penicillin administered did not appreciably affect the incidence of serologic cures; however, the duration of treatment may have some effect. The serologic cure rates of the patients were: Group A, 25.1 percent; group B, 11.0 percent; and group C, 6.4 percent. There was a reduction of the percentage of serologic cures as the duration of treatment was shortened, even though the total dosage was constant.

No attempt is made at this time to compare the permanent results of penicillin treatment of yaws with the results previously obtained with the arsenicals and heavy metals. Nevertheless, it can be said that: (1) The lesions heal with great rapidity, and the patients are rendered noninfectious very quickly; (2) a single daily intramuscular injection of penicillin allows for the completion of therapy in a few days (this is an ideal form of therapy for Haiti where protracted schedules cause irregular attendance as well as interrupted and inadequate treatment); and (3) penicillin is certainly less toxic and much safer to use than the arsenicals.

Because it is now possible to treat yaws in a short period of time at little cost, the author believes that there is no reason for 80 percent of the rural population of Haiti to be affected with this crippling and disfiguring disease.

J. Nerv. & Ment. Dis., Richmond

*Combined treatment of symptomatic paresis with penicillin and fever produced by continuous intravenous typhoid vaccine. Vincent P. Mahoney and Steven Hammerman. 109: 133–141, Feb. 1949.

Combined treatment of symptomatic paresis with penicillin and fever produced by continuous intravenous typhoid vaccine. Vincent P. Mahoney and Steven Hammerman. J. Nerv. & Ment. Dis., 109: 133–141, Feb. 1949.

The authors present a report of the treatment of 44 patients with symptomatic paresis with combined penicillin and fever induced by continuous intravenous typhoid vaccine. Twenty-eight patients were Negroes. There were 37 male and 7 female patients whose ages varied from 23 to 55. Many of the patients had received heavy metal and iodides previously, but none had received penicillin or fever therapy.

The patients treated were in the overwhelming majority grossly psychotic with marked neurologic defects, in addition to the serologic findings of paresis. In many instances because of malnutrition, dehydration, and uncooperativeness, it was necessary to restore a measure of physiologic equilibrium before beginning treatment. In this connection, electroshock therapy proved to be of immense value, and in some instances was thought to be a life-saving procedure.

Each patient received a total of 4.8 million units of penicillin both before and after fever therapy at a dosage schedule of 60,000 units intramuscularly every 3 hours. The typhoid vaccine used contained 1½ billion organisms per cubic centimeter (mixed typhoid, paratyphoid A, and paratyphoid B). Fever treatments were given on alternate days three times a week.

There were 4 deaths in this series of 44 patients, of which 3 (6.8 percent) may be considered as deaths due to treatment. Because of the exigencies of the situation (general psychiatric hospital overcrowding) rigid selection of patients for treatment could not be accomplished. It is believed that a more rigid criterion of selection would lower the mortality figure.

Statistical data on clinical and serologic results of treatment are presented in tabular form. The preliminary follow-up period has been from 1 to 10 months, with 90.8 percent follow-up obtained. Some to marked degree of clinical improvement has been obtained in 86.4 percent of patients treated, with 56.8 percent being discharged to an out-patient status. More patients will probably be able to return to useful socioeconomic status at a later date. Thirty-six of 41 cases (87.8 percent) showed some to marked spinal fluid improvement.

The only complications observed from penicillin were an occasional mild fever and malaise. The common complications encountered due to typhoid vaccine therapy were (1) persistent hyperthermia, (2) abdominal distention with urinary retention, (3) mild anemia, (4) hypoproteinemia, (5) mild hypochloremia, and (6) dehydration with incipient acidosis and azotemia. The complications to be encountered may be anticipated and with care effectively combated. Routine weekly studies plus daily clinical checks were found to be of great aid in detecting and combating complications encountered in patients in this series.

Owing to the difference in selection of cases and inevitable subjective evaluation of the degree of improvement, it is difficult to make an accurate comparison with the results of other workers.

The authors state that the use of continuous intravenous typhoid vaccine as a means of producing and maintaining fever was found practical, easily administered, and always efficacious.

J. SOCIAL HYG., NEW YORK

The state of the Union regarding commercialized prostitution. 35 : 146–160, Apr. 1949.

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Venereal diseases. 1 : 153–154, Jan. 22, 1949.

M. J. AUSTRALIA, SIDNEY

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PRESSE MÉD., PARIS

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QUART. BULL., NEW YORK

The City's health in 1948. [V. D.] 17 : 3–5, Spring 1949.

STAT. NAVY MED., WASHINGTON

Venereal disease contact investigation, first quarter—1948. Special Articles. 5 : 5–7, Jan. 1949.

UROL. & CUTAN. REV., WEST PALM BEACH

The value of the prostate and the seminal vesicles in human economy. [V. D.] Belmiro Valverde. 53 : 157–169, Mar. 1949.

Urinary extravasation. [Gonorrhea.] Clifford E. Bagley. 53 : 208–211, Apr. 1949.

Blastomycosis (Gilchrist) (North American type.) The first case on record successfully treated with penicillin. [Syphilis.] Tibor Benedek. 53 : 216–220, Apr. 1949.

Luetic myocarditis—observations of pathology and problem of establishing a true clinical entity. David N. Kremer and Howard U. Kremer. 53 : 220–221, Apr. 1949.

STATISTICS

Cases of Congenital Syphilis Reported to the Public Health Service, Fiscal Years 1941–49, by Quarters

[Known military cases excluded]

Fiscal Period	Continental United States	United States, including Territories
1941: First quarter	4, 380	4, 396
Second quarter	3, 936	3, 949
Third quarter	4, 410	4, 423
Fourth quarter	4, 866	5, 184
Total	17, 592	17, 952
1942: First quarter	4, 220	4, 763
Second quarter	4, 180	4, 708
Third quarter	4, 110	4, 513
Fourth quarter	4, 414	4, 937
Total	16, 924	18, 921
1943: First quarter	4, 405	4, 824
Second quarter	3, 861	4, 349
Third quarter	3, 829	4, 229
Fourth quarter	4, 078	4, 540
Total	16, 173	17, 942
1944: First quarter	3, 630	4, 368
Second quarter	3, 102	3, 450
Third quarter	3, 442	3, 875
Fourth quarter	3, 402	4, 014
Total	13, 576	15, 707
1945: First quarter	3, 110	3, 795
Second quarter	2, 853	3, 361
Third quarter	3, 006	3, 543
Fourth quarter	3, 370	4, 031
Total	12, 339	14, 730
1946: First quarter	3, 035	3, 453
Second quarter	2, 684	3, 187
Third quarter	3, 042	3, 683
Fourth quarter	3, 345	3, 858
Total	12, 106	14, 181
1947: First quarter	3, 049	3, 473
Second quarter	3, 033	3, 453
Third quarter	3, 067	3, 589
Fourth quarter	3, 135	3, 612
Total	12, 284	14, 127
1948: First quarter	3, 140	3, 480
Second quarter	2, 871	3, 111
Third quarter	3, 398	3, 668
Fourth quarter	3, 900	4, 251
Total	13, 309	14, 510
1949: First quarter	3, 536	3, 891
Second quarter	3, 097	3, 500
Third quarter	3, 695	4, 016

Source: Form 8958-B FSA—PHS—Division of Venereal Disease, Office of Statistics, 6/28/49 (ML-MC)mw.

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DOCUMENTS SECTION

The JOURNAL of VENEREAL DISEASE INFORMATION

Volume 30 October 1949 Number 10

ORIGINAL ARTICLES

Attitude of Venereal Disease Patients Toward Clinics and Rapid Treatment Centers 275
Lida J. Usilton, *Public Health Administrator*
John W. Morse, *Biostatistician*

Case Holding in Out-Patient Therapy of Syphilis. A Study of Case-Holding Experiences in the Out-Patient Management of Patients Treated with Penicillin on an Ambulatory Basis 281
R. M. Sorenson, M. D., C. P. H.
R. D. Shannon, *Health Program Representative*

Rapid Treatment of Syphilis. A Second Study of Clinic Attendance . 285
Charles R. Hayman, M. D., M. P. H.

The Use of a Multiple-Copy Form as an Efficient Clerical Basis for Medical Clinics Operation 288
Henry Eisenberg, *Senior Surgeon (R)*
Robert Grund
Carma Rohwedder
Mary Elizabeth Laughlin

Characteristics of the Cerebrospinal Fluid in Lymphogranuloma Venereum 291
Laurence Finberg, *Senior Assistant Surgeon*
Richard E. Lord, M. D.
Mark T. Cenac, M. D.

CURRENT NOTES AND REPORTS 294

CURRENT LITERATURE 297

STATISTICS

Cases of Syphilis and Gonorrhea Reported by State and Territorial Health Departments, January–March 1949 306

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Public Health Service

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In order to facilitate the handling of manuscripts submitted for publication in the JOURNAL OF VENEREAL DISEASE INFORMATION, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the JOURNAL, and should be presented on separate sheets, rather than within text material.

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Attitude of Venereal Disease Patients Toward Clinics and Rapid Treatment Centers[1]

Lida J. Usilton, M. A., Public Health Administrator, and John W. Morse, M. A., Biostatistician, United States Public Health Service

Introduction

Two factors prompted this study of attitude of patients toward health department venereal disease clinics and rapid treatment centers: (1) recognition of the fact that, from a case-finding point of view, persons making use of the facilities should be so favorably disposed in attitude that they will neither fail to return for necessary diagnosis and treatment nor hesitate to recommend the facilities to others, and (2) the desire to find out how satisfactory the services were and what failures existed, in the opinion of those using them, so that corrective action could be taken.

Method of Study

During the latter part of 1947, questionnaires were developed to meet the above-mentioned objectives. Seven States participated in the study, sending in a total of 1,668 completed questionnaires by the end of 1948. Effort was made to insure confidence—no names were requested on the form, privacy was assured, and the form itself was given in a folded condition to the respondent upon leaving the clinic or center, being returned in most areas to a "ballot box." The questionnaires were given to all treatment center patients and, in the clinics, to patients as well as persons who reported for diagnosis. All questionnaires distributed were actually completed, either by the patients themselves or by an interviewer in cases of illiteracy. There was no selectivity of patients and no sampling involved. The findings can therefore be considered as representative, there being no biased selection of "gripers" or sampling errors.

The questionnaire, simple in design, was a single form involving eight questions for use in the clinics and six for use in the treatment centers. Both forms requested not only background information (sex, race, and age), but also provided for the recording of any criticisms or complaints, the extent to which the item most criticized bothered the respondent, and an over-all appraisal of conditions. For those who might be hesitant to criticize, a loophole was provided by including a question as to whether the respondent had heard any other persons complain about the clinic or center. The questionnaire thus provided for the recording of specific criticisms and certain background characteristics of the respondent, in addition to a measure of the patient's attitude.

Whereas the analysis of specific criticisms required only straightforward tabulation, the measurement of attitude involved the establishment of an attitude scale. For both clinic and treatment center questionnaires, two basic decisions had to be made regarding each question: (1) whether it contained components which reflected the respondent's attitude toward the clinic or treatment center, and (2) what type of question response best reflected this attitude.

All questions considered as reflecting attitudes were cross-tabulated with each other. Coefficients of association were computed for each cross-tabulation and for all possible combinations of replies. Those questions and their particular response classifications which yielded relatively high coefficients of association were decided upon as reflecting, in combination, the attitude toward the clinic or center. The five questions thus selected formed a battery, each probing at the attitude from a different angle. These questions were combined to provide a single score: patients answering all five unfavorably were given a score of 5; those answering any four questions unfavorably were given a score of 4, and so on; those answering none unfavorably were scored 0. Fortunately, the same questions and responses could be used in scoring both clinic and treatment center questionnaires, thus permitting comparisons of the average scores between clinics, centers, and age groups.

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[1] From the Division of Venereal Disease.

The fact that reactions, on the whole, were quite favorable toward both clinics and rapid treatment centers affords much encouragement; however, certain internal comparisons of the data and the criticism tabulations may be of help in bettering the services.

Attitude

In figure 1, which shows the attitude toward clinics and rapid treatment centers, the vertical scale should be considered as an index of unfavorable attitude, being nothing more than the average number of attitude questions answered unfavorably. On this basis, it is shown that attitudes in the youngest age group, in both clinics and treatment centers, are about four times as unfavorable as attitudes in the oldest age group. This finding, important from a case-finding point of view, shows that everything possible should be done to insure good favor in the young age groups, since these young people, once served, may relapse or become reinfected; also, their attitudes may be

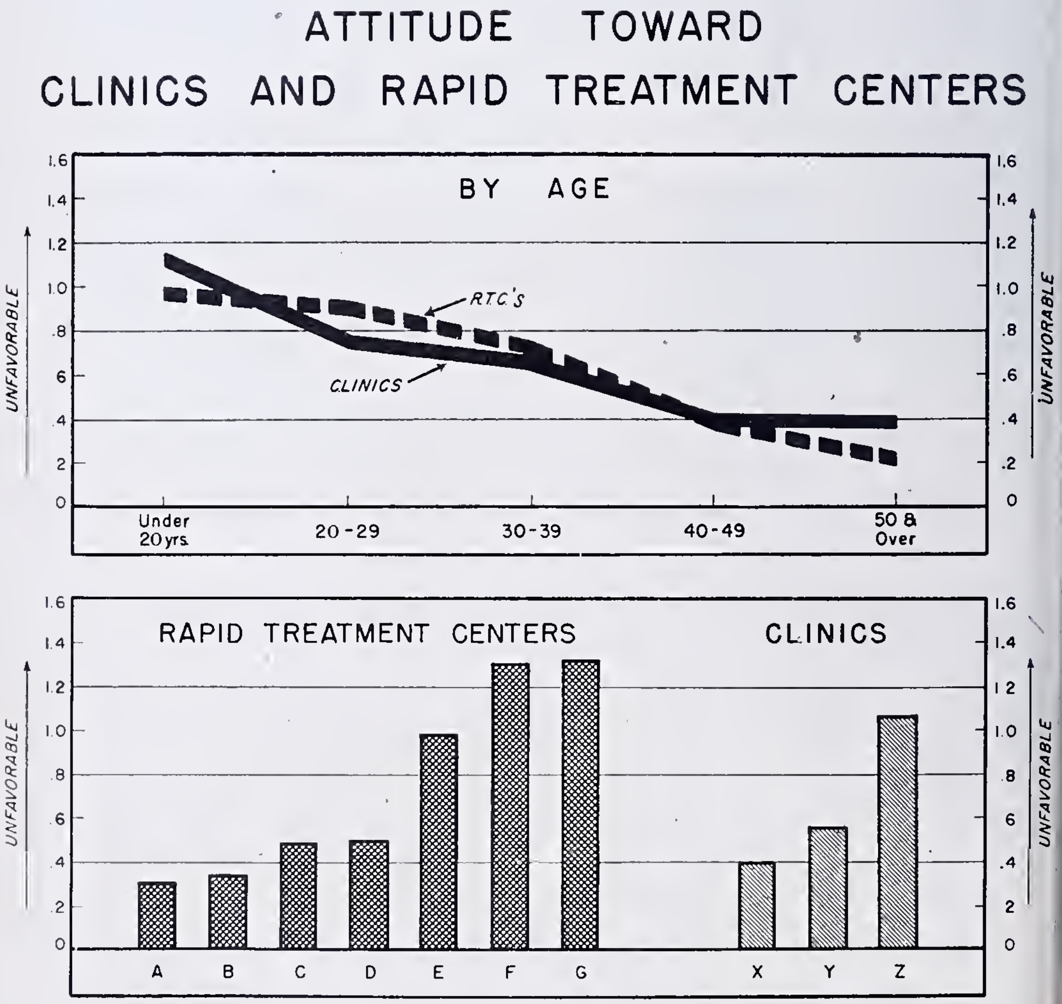

FIGURE 1.

passed on to contemporaries—the age group with high syphilis incidence.

The fact that there were such large differences (bottom of fig. 1) from clinic to clinic and among treatment centers indicates the possibility for improvement.

Tables 1 and 2 show that unfavorable attitudes may have more bearing on the case-finding program than was thought possible. Of the 835 persons questioned at clinics, 8.5 percent said that they would not recommend the clinic to a person who needed an examination for venereal disease, while 4.1 percent of 833 persons questioned at treatment centers checked "No," that they would not recommend the center to a person who needed treatment (table 1).

At the clinics, persons were also questioned as to whether they had ever recommended the clinic to anyone (table 2). The fact that 42 percent had so recommended the clinic indicates that recommendation in talk with others may be an important factor in the case-finding program.

Table 1.—*Percentage distribution of responses*

Persons questioned in clinics

If you knew anyone who needed an examination for VD, would you recommend this place to him?

(Number questioned)	(835)
	Percent
Yes	88. 5
Yes, qualified	. 4
No	8. 5
Not answered	2. 6
Total	100. 0

Persons questioned in treatment centers

If you knew anyone who needed treatment for VD, would you recommend this place to him?

(Number questioned)	(833)
	Percent
Yes	95. 2
Yes, qualified	. 1
No	4. 1
Not answered	. 6
Total	100. 0

Table 2.—*Percentage distribution of responses—persons questioned in clinics*

Have you ever recommended this clinic to anyone?

	Percent
Yes	42. 0
No	49. 4
Not answered	8. 6
Total	100. 0

Further evidence to indicate the importance of word-of-mouth advocacy of diagnostic facilities is shown in data resulting from the administration of another questionnaire[2] to persons with primary and secondary syphilis in a treatment center (table 3). In contrasting the responses of cases brought to diagnosis through contact investigation or some required test (nonvolunteers) with those coming to diagnosis of their own accord (volunteers), it can be seen that for both groups a large percentage had talked over their trouble or symptoms before their examination, relatively more of the volunteers having done so. As to the advice received, the volunteers tended to get better information, notwithstanding the fact that 1 out of the 65 who had talked with others was told, "Don't go to the clinic."

The Criticisms

Two methods of improving the attitudes of those served by clinics and treatment centers exist: (1) to propagandize, and (2) to take into account and to correct shortcomings which may have contributed to the formation of unfavorable opinions. Tables 4, 5, and 6 present in summary fashion the specific criticisms noted on the interview forms. Whereas

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[2] This questionnaire was designed to study the differences between volunteer and nonvolunteer patients.

Table 3.—*Response of patients with primary and secondary syphilis*

Did you talk over YOUR trouble or symptoms with anyone before you went to the doctor or to the clinic?

	Volunteer	Nonvolunteer
(Number questioned)	(118)	(116)
	Percent	*Percent*
Didn't know had trouble	0	25. 8
No	44. 9	37. 1
Yes	55. 1	37. 1
Total	100. 0	100. 0

(If yes) What did this person or any of these persons suggest that you do about your trouble? (Multiple answers possible)

	Volunteer	Nonvolunteer
(Number questioned)	(65)	(42)
	Percent	*Percent*
Go to doctor	20. 0	4. 8
Go to clinic	16. 9	11. 9
Go to RTC	20. 0	16. 7
Go to health department	20. 0	35. 7
Go to medical attention (not specific)	18. 5	23. 8
Drugstore or home remedies	4. 6	7. 1
Delay diagnosis, await developments	1. 5	2. 4
Don't go to clinic	1. 5	0

Table 4.—*Summary of criticisms of clinics and treatment centers*

	Clinics	Treatment centers
Number of patients filling out questionnaires	835	833
Number of patients listing criticisms	233	340
Number of criticisms	287	470
Number of criticisms per patient questioned	. 34	. 56
Persons mentioned in connection with criticisms (percent of total criticisms):	*Percent*	*Percent*
Physicians	7. 0	1. 1
Nurses	1. 7	3. 4
Medical students	3. 5	--------
Investigators	. 4	--------
General personnel	3. 8	1. 1
Other patients	. 3	4. 4
Total referring to persons	16. 7	10. 0
No person mentioned [1]	83. 3	90. 0
Total	100. 0	100. 0

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[1] The form did not suggest that persons be mentioned in connection with the criticism. The tabulation is then that of free response.

Table 5.—*Criticisms of clinics*

	Percent distribution of 287 criticisms	
Handling of patients	37.3	
Wait in line too long		26.8
Personal attitude of some staff members		3.5
Mixing of sexes; mixing of races		2.8
Discourteous or unfriendly; rough		2.1
Not enough time given; tardiness in starting clinic session		2.1
Treatment	23.4	
Hurts (reference to needles or shots)		7.7
Hurts (no reference to needles or shots)		4.9
Takes too long		4.5
No good; poor or improper nursing or medical care		3.5
Make you come back		2.8
Conditions (physical and personal)	19.4	
Privacy in examining room		4.9
Unclean; location; comfort facilities		4.5
Understaffed		2.4
Organization		2.4
Give your name; people talk, meet people you know		2.4
Miscellaneous		2.8
Patient education:		
“They don’t tell enough”	7.7	
Clinic hours:		
More night hours; more days open; not enough hours	7.7	
Posttreatment observation:		
Too long a period; not often enough; too often	2.8	
Diagnosis:		
Takes too long; poor or improper	1.7	
Total	100.0	

some of the items may be corrected by direct attack, there are some which may require indirect action. For example, while further reduction of waiting time in a clinic may be financially impossible, even after a review of administrative procedure and physical set-up, the waiting time may be made to seem shorter by the provision of reading material, music, or educational movies, as is done in some clinics.

These tabulations of criticisms, while representative only for the areas participating in this study, may be of value in pointing out conditions which generally bother persons who make use of clinics and treatment centers. Duplication of this type of study is unnecessary to determine what particular criticisms are prevalent in a particular clinic or center. This study, which has attempted to point out the importance of such investigation, has given an indication of shortcomings in several facilities. Considerable information might be secured by areas interested in their patient relations by the use of a suggestion box which could be used by patients to vent their criticisms. A summary of such suggestions and/or criticisms, while not representative for a particular clinic or center, might provide useful information upon which action could be taken.

Summary

This report describes a study in which 1,700 persons in clinics and rapid treatment centers in 7 States were questioned in order to determine their attitudes toward these facilities. The results of this investigation, which show that the attitudes of persons served in clinics and treatment centers do have some indirect

Table 6.—*Criticisms of rapid treatment centers*

	Percent distribution of 470 criticisms	
Food	29. 0	
Treatment	20. 8	
Hurts (reference to needles or shots)		10.
Hurts (no reference to needles or shots)		6.
Takes too long; poor or improper nursing or medical care		2.
Type of treatment		1.
Posttreatment observation too long		.
Policies	16. 2	
Visitor restrictions		4.
Rules and regulations (or lack of them)		4.
Patients working		3.
Liberty		3.
Handling of patients	6. 8	
Personal attitude of staff		3.
Mixing of races; mixing of sexes		2.
Wait in line too long; rough		.
Miscellaneous conditions (physical and personal)	27. 2	
Reading facilities		5.
Comfort facilities		3.
Unclean		3.
Noise; lack of rest		3.
Bed linens		3.
Organization or management		1.
Other		6.
Total	100. 0	

bearing on the venereal disease case-finding program, disclosed the following facts:

1. In general, the attitudes of patients toward both clinics and treatment centers are quite favorable.

2. There are large differences in the attitudes of persons from clinic to clinic and among treatment centers, thus indicating possibilities for improvement.

3. Attitudes of patients in the youngest age group, in both clinics and centers, are about four times as unfavorable as are those of patients in the oldest age group, a finding which is in contrast with the desirability of insuring good favor particularly in the young group in which early syphilis is more prevalent.

4. Of persons in clinics, 8.5 percent said that they would not recommend the clinic to persons who needed an examination for venereal disease.

5. About 4 percent of the treatment center patients said that they would not recommend the center to anyone who needed treatment.

6. Word-of-mouth advice was an important factor in getting infected persons to seek diagnosis; holding conditions for criticism to a minimum and creating favorable attitudes are therefore important from a case-finding point of view.

7. Detailed tables are presented summarizing the specific criticisms mentioned.

8. It is indicated that this type of investigation might be profitable in other areas through the use of a "suggestion box."

Case Holding in Out-Patient Therapy of Syphilis[1]

A Study of Case-Holding Experiences in the Out-Patient Management of Patients Treated With Penicillin on an Ambulatory Basis

R. M. Sorenson, M. D., C. P. H.,[2] and R. D. Shannon, Health Program Representative[3]

On September 1, 1948, the Bureau of Health and Hospitals of the City and County of Denver discontinued the operation of a rapid treatment center for syphilis and replaced it with a combination of in-patient care in the medical wards of the Denver General Hospital and ambulatory treatment in the out-patient department.

This report represents the case-holding effectiveness experience from September 1, 1948, through February 1949, and includes the first 200 patients treated on an ambulatory basis during that period. Treatment consists of single daily injections of 600,000 units of procaine penicillin in oil with 2 percent aluminum monostearate. Of the 200 patients, 188 were scheduled for treatment for a period of 10 days and were scheduled to receive 6 million units. In some instances, depending on the findings in the individual case, patients with central nervous system syphilis were given as much as 12 million units in a period of 20 days. In 3 cases of congenital syphilis, the dosage was adjusted for the weight of the patient, 2 being given 3 million units and 1, 1.5 million units. The group studied in this report represents a fairly good cross section of our clinic population. It is about equally divided between the sexes. Thirty-five percent of the group were white, 35 percent were colored, and 30 percent were Spanish-American; no one section of the group reflected a greater tendency to following the scheduled course of treatment than any other.

Table 1 shows the effectiveness of case holding in relation to the type of schedule employed and indicates that, regardless of the length of treatment time, 78 percent of the patients completed treatment on schedule without a single lapse from treatment. An additional 12 percent completed treatment with one or more lapses.

Table 1.—*Case holding, by length of treatment schedule*

Treatment status	Total patients		10-day schedule		15-day schedule		20-day schedule	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Completed treatment on schedule, no lapse	156	78.0	146	77.7	7	77.8	3	100.0
Completed treatment with one or more lapses	24	12.0	23	12.2	1	11.1	-------	-------
Patients completing treatment in clinic	180	90.0	169	89.9	8	88.9	3	100.0
Patients completing treatment elsewhere	6	3.0	6	3.2	-------	-------	-------	-------
Total patients completing treatment	186	93.0	175	93.1	8	88.9	3	100.0
Failed to complete treatment	11	5.5	11	5.9	-------	-------	-------	-------
Treatment discontinued	3	1.5	2	1.0	1	11.1	-------	-------
Total patients	200	100.0	188	100.0	9	100.0	3	100.0

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[1] From the Bureau of Health and Hospitals, City and County of Denver, Colo.; James P. Dixon, M. D., Director.

[2] Director, Division of Venereal Disease Control, Bureau of Health and Hospitals, City and County of Denver, Colo.

[3] U. S. Public Health Service.

Ninety percent of all patients completed treatment in the originating clinic and required little or no case-holding management. Of the 24 cases completing treatment with one or more lapses, 16 had a lapse of 1 day only, and 4 had a lapse of but 2 days. The remaining 4 patients had lapses ranging from 3 to 5 days, with 1 patient requiring a second course of treatment, which was completed in the scheduled 10 days with no lapse. The 6 patients who completed treatment elsewhere probably represent case-holding failures, in that 4 of them were transferred to inpatient care because there was reason to suspect that they were unwilling to continue on an ambulatory basis and 2 completed treatment in another clinic and in jail, respectively.

There were 11 patients who failed to complete the prescribed schedule of treatment. Nine of these received 5.4 million units and 2 received 4.8 million units, and 4.2 million units respectively.

Of the three on whom treatment was discontinued, two received 4.8 million units. Treatment of the third, a case of syphilitic aortitis with insufficiency, was discontinued when severe tachycardia, dyspnea, and moderate generalized edema appeared after the administration of 1.8 million units of penicillin.

The group of patients studied were nearly equally divided as to sex; 55 percent were males and 45 percent were females. Table 2 indicates that nearly the same percentage of men and women completed treatment on schedule.

A large number of patients had had some form of previous treatment—63 percent as compared with 37 percent who had had no previous treatment. Nevertheless, almost equal percentages of both groups completed treatment as pre-

Table 2.—*Case holding, by sex*

Treatment status	Total patients	Males		Females	
		Number	Percent	Number	Percent
Completed treatment on schedule, no lapse	156	88	79.3	68	76.4
Completed treatment with one or more lapses	24	12	10.8	12	13.5
Patients completing treatment in clinic	180	100	90.0	80	89.9
Patients completing treatment elsewhere	6	2	1.8	4	4.5
Total patients completing treatment	186	102	91.9	84	94.4
Failed to complete treatment	11	6	5.4	5	5.6
Treatment discontinued	3	3	2.7	----	----
Total patients	200	111	100.0	89	100.0

Table 3.—*Case holding, by previous treatment status*

Treatment status	Total patients	Patients who had previous treatment		Patients who had no previous treatment	
		Number	Percent	Number	Percent
Completed treatment on schedule, no lapse	156	98	77.8	58	78.4
Completed treatment with one or more lapses	24	18	14.3	6	8.1
Patients completing treatment in clinic	180	116	92.1	64	86.5
Patients completing treatment elsewhere	6	3	2.4	3	4.0
Total patients completing treatment	186	119	94.5	67	90.5
Failed to complete treatment	11	5	4.0	6	8.1
Treatment discontinued	3	2	1.5	1	1.4
Total patients	200	126	100.0	74	100.0

scribed. Table 3 indicates previous treatment alone is not a factor in case holding.

It will be noted from table 4 that a greater percentage of patients with late latent and late syphilis finished treatment on schedule than did those with other stages of the disease. A greater percentage of patients with early syphilis completed treatment with one or more lapses than did those with late syphilis. The total percentage of patients completing treatment shows very little difference by stage of disease.

In table 5 the cases have been tabulated by age. There is a tendency for more of the older patients than of the younger patients to complete treatment on schedule. More of the younger patients completed treatment with one or more lapses. The total number of patients completing treatment varied little by age.

Discussion

It is probable that several factors combine to produce the tendencies noted in tables 4 and 5. In the first place, the patients with late latent and late syphilis have for the most part been subjected to many and varied types of treatment over a considerable period of time and

Table 4.—*Case holding, by stage of disease*

Treatment status	Diagnosis of syphilis							
	Primary or secondary		Early latent		Late and late latent		Congenital	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Completed treatment on schedule, no lapse	22	68.8	42	73.7	87	83.8	5	71.4
Completed treatment with one or more lapses	5	15.6	8	14.0	10	9.6	1	14.3
Patients completing treatment in clinic	27	84.4	50	87.7	97	93.4	6	85.7
Patients completing treatment elsewhere	2	6.2	2	3.5	1	1.0	1	14.3
Total patients completing treatment	29	90.6	52	91.2	98	94.4	7	100.0
Failed to complete treatment	3	9.4	5	8.8	3	2.8	0	
Treatment discontinued	0		0		3	2.8	0	
Total patients	32	100.0	57	100.0	104	100.0	7	100.0

Table 5.—*Case holding, by age*

Treatment status	Total patients	Age											
		Less than 15		15–24		25–34		35–44		45–54		55 and over	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Completed treatment on schedule, no lapse	156	4	80	39	72.2	34	70.8	31	79.5	24	82.7	24	96.0
Completed treatment with one or more lapses	24	1	20	8	14.8	7	14.6	3	7.7	5	17.3		
Patients completing treatment in clinic	180	5	100	47	87.0	41	85.4	34	87.2	29	100.0	24	96.0
Patients completing treatment elsewhere	6			3	5.6	2	4.2	1	2.6				
Total patients completing treatment	186	5	100	50	92.6	43	89.6	35	89.8	29	100.0	24	96.0
Failed to complete treatment	11			4	7.4	3	6.2	4	10.2				
Treatment discontinued	3					2	4.2					1	4.0
Total patients	200	5	100	54	100.0	48	100.0	39	100.0	29	100.0	25	100.0

are therefore quite anxious to avail themselves of a form of treatment that offers an end to further treatment. Secondly, this same group of patients had more than one exposure to patient education by virtue of the fact that they had had syphilis over a period of years.

By contrast, most of the younger age group had early syphilis and therefore seldom had but a single exposure to patient education. Every patient is interviewed by the public health nurse prior to treatment, at which time a complete interpretation of syphilis is given to the patient and the necessity for continuous treatment emphasized. If a patient lapses from treatment he is contacted on the day following his lapse, and at that time the salient features of the original interview are reemphasized. The effectiveness of such a procedure is shown by the percentage of cases of early syphilis induced to complete treatment. It may therefore be assumed that the quality and quantity of patient interviews are factors which favor completion of treatment.

It should be pointed out that optimum conditions for completion of treatment according to prescribed schedules exist in this clinic and may be a contributing factor to the high percentage of completely treated patients. To begin with, Denver General Hospital is a part of the Bureau of Health and Hospitals, and the venereal disease clinic is operated within the hospital. The very close operational and geographic integration provides for a directness of action that may not be possible under other circumstances. Secondly, if the patient cannot attend the clinic during its hours of operation, arrangements are made to give treatment in the emergency room of the hospital at any hour the patient can present himself. In this clinic, therefore, there remains very little but the patient's unwillingness or his lack of understanding of the value to be derived from treatment to keep him from completing treatment on schedule.

A screening process designed to insure complete treatment for all patients by eliminating the obviously uncooperative patient from ambulatory treatment and placing him on in-patient care is used in this clinic. Others are hospitalized because of physical reasons or because they have no means with which to care for themselves while being treated. Still others come from points some distance from Denver and are hospitalized. At first glance this process of selection might seem to be a procedure which might bias the results we have reported. During the period covered by this report, a total of 43 patients were hospitalized. Of these, 20 (46.5 percent) were referred from areas outside of Denver; 15 (35 percent) were hospitalized for physical reasons or were given a type of treatment, such as fever, that made ambulatory treatment impracticable; and 8 (18.6 percent) were judged to be unreliable to the extent that completion of an ambulatory treatment schedule would be unlikely. The fact that the first group came to us voluntarily, sometimes from distances of several hundred miles, and wanted treatment is prima facie evidence of a desire to follow direction. The second group needed special treatment or were so ill that they were left little choice but to follow directions. These two groups, totaling 35 patients (81.5 percent) compare favorably with figures set forth in table 1, on the basis of which we would have expected 34 patients (78 percent) to complete treatment on schedule.

On the basis of this study, it seems reasonable to assume that the management of ambulatory therapy does not present a major case-holding problem to clinics operating on a daily basis if the treatment schedule can be fitted into the patient's daily routine and if the obviously uncooperative patient is eliminated. Under such conditions, the patient will, in 9 cases out or 10, complete his treatment in the prescribed time.

Summary and Conclusions

1. Ambulatory treatment of syphilis with daily administration of slowly absorbed penicillin offers a convenient method of completing treatment in a high percentage of patients.

2. Total treatment time up to 20 days, sex, and previous treatment do not appear

to be important factors in case-holding efficiency.

3. Age of the patient and stage of disease seem to influence the percentage of patients completing treatment schedules as outlined. Older patients and those with later stages of syphilis had better records.

4. Because of differences in patient education, it is felt that this factor is more responsible for good case holding than is either the age of the patient or the stage of disease. This study, then, points up the importance of good patient education, especially in those patients to whom the acquisition of syphilis is a new experience. It would also appear that the number of cases completing treatment is in direct proportion to the amount of patient education.

5. It is desirable to have treatment facilities so arranged that treatment can be fitted to the patient's daily routine.

6. Of the syphilis patients of the Denver General Hospital for whom out-patient treatment is suitable, ambulatory treatment does not present a major case-holding problem.

Rapid Treatment of Syphilis

A Second Study of Clinic Attendance

Charles R. Hayman, M. D., M. P. H., Deputy State Health Officer, Delaware

"The favorable clinical and serologic response of early syphilis to 3 days of penicillin therapy may be the key to the solution of the time factor in the ambulatory management of syphilis" (*1*). Until such favorable response is demonstrated, however, daily injections of slowly absorbed penicillin should be given for periods of 6 to 14 days. It is important to know whether patients receiving such treatment on an out-patient basis will attend all scheduled days.

In January 1947, with the aid of a grant from the United States Public Health Service, we began the rapid treatment of syphilis on an out-patient basis, using a daily injection of penicillin in oil-beeswax. An initial report on 123 patients (*2*), on 6-, 7-, 8-, and 10-day schedules, showed that 108 patients attended all scheduled days, 11 patients missed 1 day, and 3 patients missed 2 days.

The study has been continued to May 1949, with the treatment of an additional 150 cases. This report is a summary of the 273 patients treated.

Classification of Patients

The age range was from 5 to 67 years. Ninety-two percent of the patients were colored. Sixty-four percent were female. Nine women were pregnant.

There were 157 new clinic patients (patients admitted to the Kent County clinics less than 3 months before receiving the first penicillin treatment). Of these, 10 had primary and 30 had secondary syphilis. These patients received a weekly injection of arsenic until such time as penicillin treatment was started. None lapsed during this period.

However, more than two-thirds of our new patients with primary and secondary syphilis were not given ambulatory treatment but were sent to the Welfare Home in Smyrna for in-patient treatment. This was done whenever the patient would consent to go and whenever a bed was available.

There were 116 old clinic patients who had received arsenic and bismuth treatments over a period of 3 months to several years. Fifty-seven of these had been highly delinquent in taking treatments.

In the series reported in 1947, only 42 were new cases, and 81 were old cases. One of our purposes in giving rapid treatment was to clear the clinic of these old patients. That this was successful is shown by the composition of the second series, of which 115 were new cases and 35 were old.

Procedure

Rapid treatment sessions were held whenever a group of 10 or more suitable patients had accumulated in each of our clinics. These were held as follows: 10 sessions in Dover for 167 patients, 2 in Milford for 51, 1 in Smyrna for 12, and 1 in Felton for 7. Two sessions were held in Sussex County on a demonstration basis: 1 in Georgetown and 1 in Seaford for 18 patients each. The sessions began on Monday and continued daily except Sunday. Almost all cases were given a daily dose of 600,000 units of penicillin in oil-beeswax. Treatment was always administered by a physician. The doctor and the nurse reminded each patient daily of the importance of regular attendance.

Findings

Of 273 patients on 6-, 7-, 8-, and 10-day schedules, 27 missed 1 day, 8 missed 2 days, and 3 missed 3 or more days (table 1). On the 6-, 7-, and 8-day schedules, 149 out of 160 patients attended all scheduled days (93 percent), whereas, on the 10-day schedule, only 86 out of 113 patients attended all days (76 percent). The difference is significant.

The particular days of treatment missed are shown in table 2. It is significant that absences were not more frequent in the last days of the sessions, in view of the fact that more than half of the patients had some soreness of the buttocks and stiffness of the muscles, which apparently increased with each successive injection.

Reasons for Absence

Thirty-eight patients missed one or more days of treatment. No definite reason can be assigned for 24 persons. Five misunderstood when the sessions would be started and attended regularly from the second day. Four could not obtain transportation from rural areas on certain days. Two arrived late to the clinic.

Table 1.—*Number of days of treatment missed*

Schedule	Number of patients treated	Number of days missed			
		0	1	2	3 or more
6-day	52	50	1	0	1
7-day	90	82	8	0	0
8-day	18	17	0	1	0
10-day	113	86	18	7	2
Total	273	235	27	8	3

Table 2.—*Particular treatment day missed*

Schedule	Number of patients treated	Treatment day missed									
		1	2	3	4	5	6	7	8	9	10
6-, 7-, and 8-day	160	2	1	1	2	4	4	0	0	----	----
10-day	113	6	2	3	1	3	8	4	5	7	3
Total	273	8	3	4	3	7	12	4	5	7	3

Table 3.—*Number of days of treatment missed minus extra days attended*

Schedule	Number of patients treated	Number of days missed minus extra days attended			
		0	1	2	3 or more
6-, 7-, and 8-day	160	156	4	0	0
10-day	113	94	10	7	2
Total	273	250	14	7	2

One had a severe general urticaria on the ninth and tenth days, necessitating bed rest. One person, with probable cardiovascular syphilis, had chest pain, and treatment was discontinued after 3 days. One patient was delivered at home after 3 days, and treatment was completed there.

Extra Days Attended

Thirteen patients who had missed 1 day were asked to attend an extra day at the end of the session; all responded. One patient who had missed 2 days made them up.

Because clinic space was needed for other work, this procedure of extra days was not done routinely, and only early cases in the more recent sessions were asked to make up missed days. The good response, however, indicates the possibility of completing almost all treatments by adding two make-up days to each schedule (table 3). A similar conclusion was reached by Aiken (*3*) in a study of out-patient treatment by private physicians.

Summary

1. Two hundred seventy-three patients were treated for early and late syphilis on an out-patient basis, on 6-, 7-, 8-, and 10-day schedules.

2. Eighty-six percent of the patients completed treatment; 10 percent missed 1 day; 3 percent missed 2 days; and 1 percent missed 3 days.

3. Attendance on the 6-, 7-, and 8-day schedules was significantly better than on the 10-day schedule.

4. Treatment was discontinued in one person because of severe general urticaria; in a second, because of chest pain.

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The Use of a Multiple-Copy Form as an Efficient Clerical Basis for Medical Clinics Operation[1]

Henry Eisenberg, Senior Surgeon (R), United States Public Health Service,[2] Robert Grund,[3] Carma Rohwedder,[4] and Mary Elizabeth Laughlin [5]

The Clinics Section of the Venereal Disease Control Program of the Chicago Health Department developed a basic clerical system which has increased the efficiency of clinic operation, decreased the waiting time of patients, decreased the possibility of errors in permanent records, and increased the value of each employee day.

It is not the intention of this article to outline the exact procedure developed for each clinic of this Clinics Section, since details vary slightly from clinic to clinic, but rather to describe the general operation and benefits of the multiple-copy card system, which might be of aid to clinics in other cities with similar problems of large case loads, unsatisfactory clinic facilities, and a decreasing medical and clerical staff.

The preliminary step in the reorganization of the clerical system was the preparation of a flow chart to clarify the bottlenecks and duplications inherent to the clerical system formerly in use, and to make it possible to analyze the weak spots to be remedied.[6] The bottlenecks were apparent immediately, and a system using two basic cards was developed which eliminated the preparation and use of from 6 to 16 forms.

When a patient first arrives at the Information Desk of the Clinic, a clerk records on a Clinic Activity Card (fig. 1) the name and address of the patient, any previous name or address, the telephone number, the former clinic chart number if the patient has had one and has the information, and any alias.

The uses of the Clinic Activity Card are as follows:

1. To locate the medical records of the patient if he has attended the clinic previously.
2. To tabulate clinic activity.
3. To serve as a morbidity report and to form the basis for subsequent statistical analysis.
4. To serve as a clerical means of following patients during subsequent visits until a diagnosis is made.
5. To serve as the basis for the preparation of the multiple-copy Clinic Registration Card, if one is to be made.

When the basic data have been recorded on the Clinic Activity Card, the card is taken to the Admitting and Record Unit, where any previous record of the patient is pulled. If there is no previous record, a multiple-copy Clinic Registration Card (fig. 2) is prepared. This multiple-copy form is prepared on an electromatic typewriter in order to make all copies legible. Use of this form minimizes the possibility of error in copying basic information. The copies are prepared in one writing, therefore, and their uses are as follows:

1. Copy 1 becomes the permanent Clinic Registration Card of the patient.

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[1] From the Venereal Disease Control Program of the Chicago Health Department in cooperation with the U. S. Public Health Service. Under the direction of Herman N. Bundesen, Senior Surgeon (R) (Inactive), U. S. Public Health Service; President, Chicago Board of Health. Under the supervision of Frederick Plotke, M. D., Chicago Venereal Disease Control Officer.

[2] Clinics Director, Chicago Venereal Disease Control Program.

[3] Business Manager, Clinics Section, Chicago Venereal Disease Control Program.

[4] Supervisor, Registry Section, Chicago Venereal Disease Control Program.

[5] Director of Statistics, Chicago Venereal Disease Control Program.

[6] With the cooperation of Mr. John W. Morse and Mr. Kenneth Revell, representatives of the U. S. Public Health Service, and a representative of a standard register manufacturing company.

2. Copies 2 and 3 are used for serologic tests.

3. Copies 4 and 5 are used for smear and culture tests.

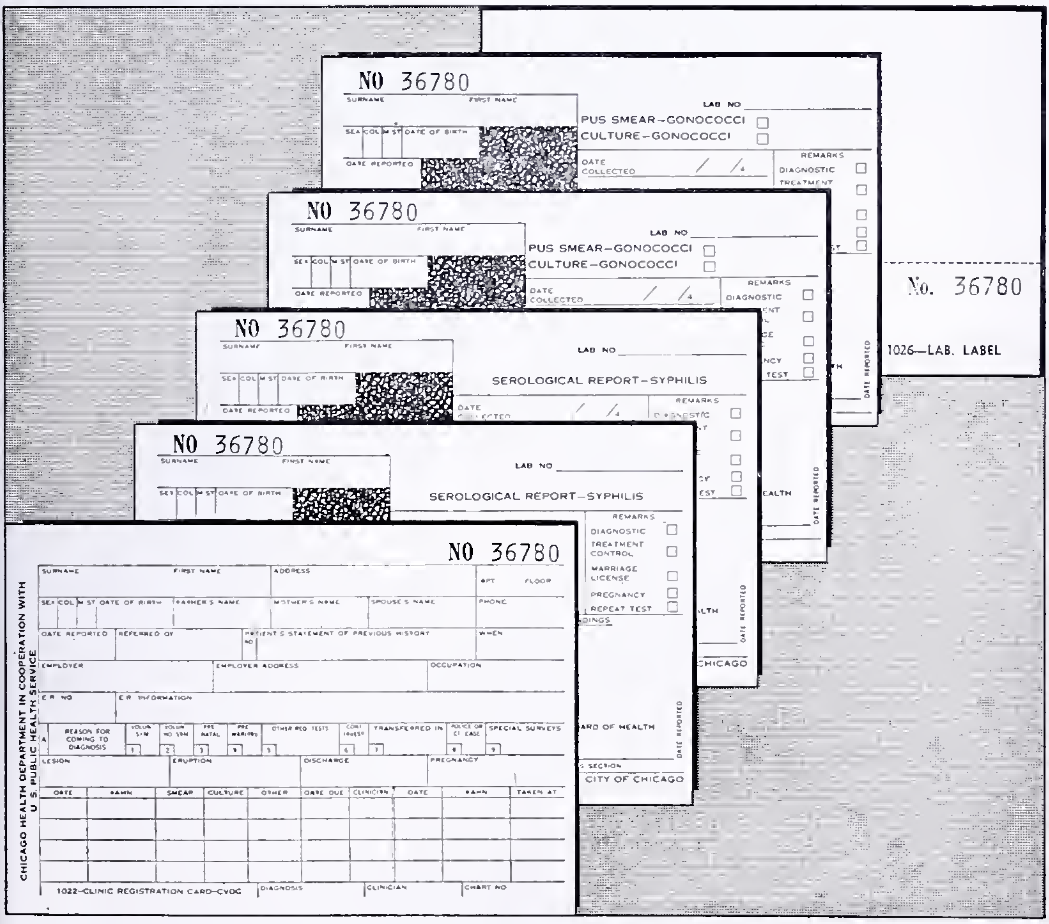
4. Copy 6 (a sheet of gummed labels) is used to identify laboratory specimens.

All multiple-copy card forms are prenumbered, and each copy in the set of forms bears the same number for identification purposes.

Copy 1, the permanent Clinic Registration Card, is filed alphabetically in a master file of clinic patients. The chart number of the patient is placed on this copy, so that it also serves as a cross file to the clinic medical chart file, where the chart of the patient is kept until 90 days after his last visit. The chart can then be filed in an inactive file, since the card remains in the master file. This first copy is a stiff card, whereas the remaining five copies are of regular paper. The remaining copies of the form, the laboratory forms, eliminate the former necessity of filling out forms one by one in longhand, which was time consuming and which allowed the possibility of many errors. Formerly, because of the length of time taken to fill out forms, the patients sometimes left the clinic before they were examined. With the use of these forms, the patient can progress through the clinic expeditiously during his first visit.

For subsequent appointments, the Clinic Activity Card is used as follows:

1. It is forwarded to the Tabulating Unit if no further visits by the patient are desired.



No. 36780

1026—LAB. LABEL

NO 36780

SURNAME | FIRST NAME

SEX | COL | M ST | DATE OF BIRTH

DATE REPORTED

LAB NO ____

PUS SMEAR—GONOCOCCI ☐

CULTURE—GONOCOCCI ☐

DATE COLLECTED / /4

REMARKS

DIAGNOSTIC ☐

TREATMENT ☐

NO 36780

SURNAME | FIRST NAME

SEX | COL | M ST | DATE OF BIRTH

DATE REPORTED

LAB NO ____

PUS SMEAR—GONOCOCCI ☐

CULTURE—GONOCOCCI ☐

DATE COLLECTED / /4

REMARKS

DIAGNOSTIC ☐

NO 36780

SURNAME | FIRST NAME

SEX | COL | M ST | DATE OF BIRTH

DATE REPORTED

LAB NO ____

SEROLOGICAL REPORT—SYPHILIS

DATE COLLECTED / /4

REMARKS

NO 36780

SURNAME | FIRST NAME

SEX | COL | M ST | DATE OF BIRTH

LAB NO ____

SEROLOGICAL REPORT—SYPHILIS

REMARKS

DIAGNOSTIC ☐

TREATMENT CONTROL ☐

MARRIAGE LICENSE ☐

PREGNANCY ☐

REPEAT TEST ☐

DATE REPORTED

CITY OF CHICAGO

NO 36780

CHICAGO HEALTH DEPARTMENT IN COOPERATION WITH U. S. PUBLIC HEALTH SERVICE

SURNAME | FIRST NAME | ADDRESS | APT | FLOOR

SEX | COL | M ST | DATE OF BIRTH | FATHER'S NAME | MOTHER'S NAME | SPOUSE'S NAME | PHONE

DATE REPORTED | REFERRED BY | PATIENT'S STATEMENT OF PREVIOUS HISTORY | NO | WHEN

EMPLOYER | EMPLOYER ADDRESS | OCCUPATION

E R NO | E R INFORMATION

A | REASON FOR COMING TO DIAGNOSIS | VOLUN SYM 1 | VOLUN NO SYM 2 | PRE NATAL 3 | PRE MARITAL 4 | OTHER REQ TESTS 5 | CONT INVEST 6 | TRANSFERRED IN 7 | POLICE OR CT CASE 8 | SPECIAL SURVEYS 9

LESION | ERUPTION | DISCHARGE | PREGNANCY

DATE	KAHN	SMEAR	CULTURE	OTHER	DATE DUE	CLINICIAN	DATE	KAHN	TAKEN AT

1022—CLINIC REGISTRATION CARD—CVDC | DIAGNOSIS | CLINICIAN | CHART NO

Figure 1.—Multiple-copy Clinic Registration Form.

2. If further visits are necessary, the card is filed in an appointment file by the future date of appointment. The appointment file is reviewed daily.

(*a*) If the patient reports, the card is pulled from the file and subsequent data added until the disposition of the case is determined. The card is then forwarded to the Tabulating Unit.

(*b*) If the patient does not report, the card and the patient's medical chart are given to the Head Clinician for a decision on follow-up of the patient. If field or administrative follow-up is recommended, the Clinic Activity Card serves to notify the Epidemiology Unit. (This procedure reduced the time required to assign cases to follow-up to 1 day from a former maximum of 2 weeks.)

The flow chart and the clerical system brought to light the fact that the physical arrangement of the clinic relative to medical functions was also not efficient or expedient, since diagnostic examination and therapy were separated physically. These were combined, and as a result the clinicians could render prompt medical service and maintain a continuous flow of patients.

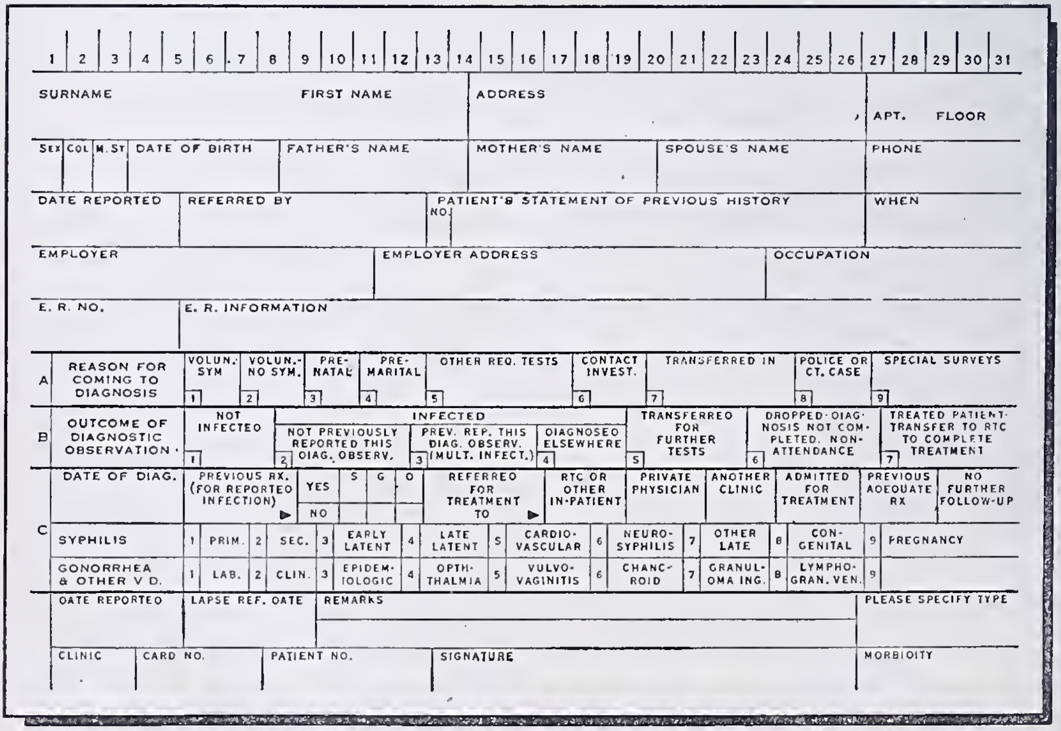
Discussion and Summary

In order to expedite the processing of patients in the Chicago Venereal Disease Control Program clinics, and to render thereby a better public health service, the Clinics Section of the Program reviewed its clerical and physical set-up.

The survey of functions and procedures and the change in methods based on the findings resulted in benefits beyond those expected. The time required for progressing a patient through the Municipal Social Hygiene Clinic (with an average of approximately 1,200 visits each day) was reduced from 3 hours to 1 hour. Personnel assigned to the Admitting and Record Unit and the personnel of the Diagnostic Unit were reduced approximately 25 percent.

Several administrative and medical advantages were gained by centralizing the Diagnostic and Treatment Units.

A multicopy form, bearing the same number on all copies, eliminated the separate preparation of registration and lab-



1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31

SURNAME
FIRST NAME
ADDRESS
APT.
FLOOR

SEX
COL
M. ST
DATE OF BIRTH
FATHER'S NAME
MOTHER'S NAME
SPOUSE'S NAME
PHONE

DATE REPORTED
REFERRED BY
NO.
PATIENT'S STATEMENT OF PREVIOUS HISTORY
WHEN

EMPLOYER
EMPLOYER ADDRESS
OCCUPATION

E. R. NO.
E. R. INFORMATION

A REASON FOR COMING TO DIAGNOSIS
1 VOLUN.-SYM
2 VOLUN.-NO SYM.
3 PRE-NATAL
4 PRE-MARITAL
5 OTHER REQ. TESTS
6 CONTACT INVEST.
7 TRANSFERRED IN
8 POLICE OR CT. CASE
9 SPECIAL SURVEYS

B OUTCOME OF DIAGNOSTIC OBSERVATION
1 NOT INFECTED
INFECTED
2 NOT PREVIOUSLY REPORTED THIS DIAG. OBSERV.
3 PREV. REP. THIS DIAG. OBSERV. (MULT. INFECT.)
4 DIAGNOSED ELSEWHERE
5 TRANSFERRED FOR FURTHER TESTS
6 DROPPED-DIAGNOSIS NOT COMPLETED. NON-ATTENDANCE
7 TREATED PATIENT-TRANSFER TO RTC TO COMPLETE TREATMENT

C
DATE OF DIAG.
PREVIOUS RX. (FOR REPORTED INFECTION) ▶

	S	G	O
YES			
NO			

REFERRED FOR TREATMENT TO ▶
RTC OR OTHER IN-PATIENT
PRIVATE PHYSICIAN
ANOTHER CLINIC
ADMITTED FOR TREATMENT
PREVIOUS ADEQUATE RX
NO FURTHER FOLLOW-UP

SYPHILIS	1 PRIM.	2 SEC.	3 EARLY LATENT	4 LATE LATENT	5 CARDIO-VASCULAR	6 NEURO-SYPHILIS	7 OTHER LATE	8 CON-GENITAL	9 PREGNANCY
GONORRHEA & OTHER V D.	1 LAB.	2 CLIN.	3 EPIDEM-IOLOGIC	4 OPTH-THALMIA	5 VULVO-VAGINITIS	6 CHANC-ROID	7 GRANUL-OMA ING.	8 LYMPHO-GRAN. VEN.	9

DATE REPORTED
LAPSE REF. DATE
REMARKS
PLEASE SPECIFY TYPE

CLINIC
CARD NO.
PATIENT NO.
SIGNATURE
MORBIDITY

FIGURE 2.—Revised Clinic Activity Card.

oratory forms, thereby reducing the possibility of clerical errors and saving the time of both personnel and patient.

A Clinic Activity Card was devised to serve as the basis for the multicopy form, as an appointment card, as a follow-up card for lapsed patients, as a morbidity report, and as a basis for statistical summaries.

Experience with these two forms and three files has resulted in a marked increase in efficiency and in employee and patient morale. The three files are:

1. An alphabetical master registration file.
2. A numerical chart file.
3. A chronological appointment file.

It is anticipated that, as a result of the objective survey of clinic operations, an increased patient load could be assimilated without detriment, as it was possible to meet a reduction in staff.

Characteristics of the Cerebrospinal Fluid in Lymphogranuloma Venereum

Laurence Finberg, Senior Assistant Surgeon, United States Public Health Service, Richard E. Lord, M. D., and Mark T. Cenac, M. D.

In the course of treating patients with venereal diseases, it was noted by one of us, as has been noted by others (*1, 2, 3*), that there were abnormalities in the protein fraction of the cerebrospinal fluid in patients having lymphogranuloma venereum. A review of the literature revealed a paucity of information on this matter. The purpose of the present study is to evaluate these abnormalities with regard to their incidence, the possible mechanism of occurrence, and their diagnostic value.

Material

The data were derived from case records of consecutive admissions of lymphogranuloma venereum patients to the United States Public Health Service Medical Center in Hot Springs National Park, Ark., beginning in January 1948. The diagnosis in all cases selected was made by or confirmed by a positive intradermal Frei test, using Lygranum antigen. In many of the cases clinical evidence of the chronic form of the disease was present.

Since other diseases coexisted in many patients, those records which revealed the presence of a condition which has been known to produce similar abnormalities in the cerebrospinal fluid were dropped from the study. This included all cases of primary and secondary syphilis and any case of neurosyphilis which had been diagnosed by history, clinical means, or laboratory evidence. Thus, any case was eliminated in which the spinal fluid Kolmer Wassermann was positive. All cases of hypertension in which the diastolic blood pressure was greater than 100 mm. of mercury, cases of advanced arteriosclerosis, and all cases in which the spinal fluid was markedly contaminated with erythrocytes, were also eliminated from consideration.

To summarize, the cases selected are those with a diagnosis of lymphogranuloma venereum, made on the basis of clinical findings or a Frei test showing greater than 9 mm. of induration and erythema, and having no evidence of any other condition which is known to produce cerebrospinal fluid abnormalities of the type herein considered.

In order that we may speak of abnormal, a standard of normal had to be set. The figures for a normal protein value may appear low to the reader, inasmuch as the cisternal fluid of Medical Center patients is routinely examined instead of the customary lumbar fluid. Merritt and Fremont-Smith set the upper limit of normal for protein in a cisternal fluid as 25 mg. percent (*4*).

Because the data on cisternal fluid have seldom been based on a large series of cases, we felt it advisable to offer as a control study 108 consecutive cases collected by the same criteria as those of the present study, with the exception that none of them had lymphogranuloma venereum. On these cases the mean value of the total protein was 15.8 mg. percent, and in all but one the colloidal mastic reading was expressed as 00000. Two cases (1.85 percent) showed elevation of total protein beyond 24.0 mg. percent. One of the latter fluids also had a mastic reading of 10000.

For purposes of this study a cisternal fluid was considered to be abnormal with regard to total protein or colloidal mastic if the former was greater than 24 mg. percent or the latter showed a positive reading in more than one tube.

Results

Out of 82 cases of lymphogranuloma venereum, 19 cases (23.2 percent) showed abnormalities in the cerebrospinal fluid (table 1), as contrasted to 1.85 percent abnormalities in a control series of 108 cases. It is noted that each of the 19 cases shows at least one positive tube in the colloidal mastic, although the reading of 10000 when it occurred as an isolated finding was not included as an abnormality.

It is further noted from the clinical signs shown in table 1 that these cases were largely in the chronic stage of the disease, with some of them being free from clinical evidence of lymphogranuloma venereum. In the total series of 82 cases no attempt could be made to break down the data by the stage of the disease. Since consecutive cases were chosen, however, some of these were cases early in the course of their infection, and these were not among those which present abnormal cisternal fluids.

Table 1.—*Nineteen cases with positive Frei tests showing abnormal cerebrospinal fluid*

	Cells per cubic milliliter	Total protein (mg. percent)	Colloidal mastic reading	Clinical signs
Normal values	0–5	7–23.9	00000	
Case No.:				
1	0	16.6	21000	Rectal stricture.
2	9	26.2	43221	Rectal stricture.
3	0	12.1	11000	Rectal stricture.
4	0	22.4	11100	Rectovaginal fibrosis and fistula.
5	0	13.4	11000	Rectovaginal fibrosis and fistula.
6	0	24.3	10000	Rectal fibrosis.
7	0	17.2	21100	Rectal fibrosis.
8	0	14.1	11000	Genital hypertrophy.
9	0	16.6	22210	Genital hypertrophy.
10	0	11.2	11000	Genital ulceration.
11	0	17.2	22000	Genital ulceration.
12	0	14.7	22100	Genital ulceration.
13	0	13.1	21000	None.
14	0	12.2	11111	None.
15	1	15.7	32100	None.
16	0	18.9	21100	None.
17	1	21.7	32100	None.
18	1	26.9	21000	None.
19	0	26.2	11000	None.

Discussion

The literature shows that the virus causing lymphogranuloma venereum was first isolated in 1930 (*5*). It was soon demonstrated that the virus diffused rapidly through the body and produced granulomatous lesions in many different organs (*6*). One specific finding was that of hyperproteinemia accompanied by hyperglobulinemia. Many of the early workers believed this to be of definite diagnostic importance (*7, 8*). This derangement of protein was found to be a permanent change, but no definite conclusions were made as to whether this indicated persistent infection (*7, 8, 9, 10*).

In 1935, Saenz (*6*) stated that recent experiments had proved an extraordinary affinity of the virus of lymphogranuloma venereum for the nervous system. Other workers showed that the inoculation into guinea pigs of the spinal fluid from patients with lymphogranuloma venereum produced typical clinical and histopathological changes of the disease in 25 percent of the guinea pigs. Sabin has stated that the virus of lymphogranuloma venereum could be the cause of severe meningoencephalitis in man (*11*).

Observations of spinal fluid changes in this disease were not found in the American literature, and very few were uncovered in the foreign literature. One article, published in 1939 (*1*), reported complete spinal fluid studies in six of eight cases. All six showed abnormalities in the colloidal mastic curve comparable to those observed in our study.

One explanation of the observed cerebrospinal fluid abnormalities is that they represent products of a local reaction, protective in nature, evoked by a low-grade meningoencephalitis resulting from viral invasion of the central nervous system. Conceivably, however, they may represent spilling over into the cerebrospinal fluid of the increased serum protein noted by many observers. The fact that the changes are largely in the first zone of the colloidal test is consistent with the hypothesis that the albumin/globulin ratio has been lowered. It will remain for electrophoretic or other fractionation studies to reveal the actual nature of the protein present.

Conclusions

1. It has been shown that a considerable number (23.2 percent) of cases of lymphogranuloma venereum manifest abnormalities of the cerebrospinal fluid. The component of the cerebrospinal fluid involved appears to be chiefly the protein, with consequent changes in the colloidal mastic test. This finding may prove to be an aid to the physician's diagnostic armamentarium, and it may conceivably represent the only indication of activity. At present, there are no data to show that such findings are an indication of activity or that they are of prognostic significance.

2. More work is needed to evaluate both the mechanism and the precise nature of the protein changes which we have observed.

3. The presence of unexplained abnormalities in the protein or colloidal tests in the cerebrospinal fluid of a patient should suggest to the clinician the possibility of lymphogranuloma venereum and warrant a Frei test.

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CURRENT NOTES AND REPORTS

Syphilis Experts Meet in United States

The World Health Organization, which is sponsoring the first international evaluation of the United States Venereal Disease Control Program, assembled seven international experts from Europe, Asia, and South America in Washington on August 15 to begin a 6 weeks' study tour of venereal disease control centers in the United States.

The WHO Expert Committee on Venereal Infections and the Public Health Service, joint organizers of the study tour, have expressed the view that study by international experts of control methods recently developed in the United States, particularly the treatment of syphilis with penicillin, and the evaluation of their effectiveness for national and international programs, would be of great value throughout the world at the present time. Among other things, it would lead to closer exchange of technics and methods between nations.

Participants were:

Dr. Juan M. Funes, Director, Rapid Treatment Center, Guatemala City, Guatemala.

Dr. E. I. Grin, Director, Zemaljski, kozno-vener, dispanzar, Ministry of Health, Sarajevo, Yugoslavia.

Dr. N. Jungalwalla, Venereal Disease Adviser to the Government of India.

Dr. Poul V. Marcussen, Director, Municipal Venereal Disease Clinic, Copenhagen, Denmark.

Dr. I. Haraszti, Chief, Venereal Disease Section, State Institute of Hygiene, Budapest, Hungary.

Dr. Sidney Laird, Adviser in Venereology, Suffolk, England.

Prof. Pierre Joulia, Professor of Skin Diseases and Syphilis, Bordeau University, Bordeau, France.

Dr. P. J. Pesare, Medical Officer in charge of Venereal Disease Education, Public Health Service, Federal Security Agency, served as medical secretary to the Commission.

After spending a full week in Washington visiting operating units of the Public Health Service Division of Venereal Disease, the Commission went to Boston, New York, Baltimore, Philadelphia, Chicago, Rochester, Hot Springs, Atlanta, Savannah, Chapel Hill, and Durham. They are then returning to Washington during the first week of October to participate in the third meeting of the WHO Expert Committee on Venereal Infections, to which it will present its official report. The meeting will be convened at the Pan-American Sanitary Bureau, the WHO Regional Office for the Americas, on October 10 through October 20.

Chicago's Program to "KO-VD"

According to a weekly report of the Chicago Health Department (July 1, 1949), the opening on June 18 of Chicago's public information campaign to "KO-VD" (knock out venereal disease) has been followed by an estimated 20 percent jump in clinic attendance. People are coming to the VD clinics at a rate of 23,000 a month, compared with a rate of 19,000 a month in May, it is stated.

All available methods are being used by the Health Department's Venereal Disease Control Program, including the following:

1. Distribution of 500,000 "KO-VD" blotters through industries, unions, and insurance companies.
2. The use of 50,000 washroom stickers with the VD message in taverns, restaurants, park rest rooms, and independent gas station washrooms.
3. Distribution in bars and taverns of 50,000 playing cards with Chinese characters translated to give the VD message.
4. The showing of two VD trailers in 40 commercial movie houses and over all television outlets in the city to an estimated audience of over a million people.
5. Display of VD advice on sheet posters, large painted signs, and car cards throughout all sections of the city.
6. Radio programs, which during the first week of the campaign included over 200 spot announcements, news releases, and 15-minute transcriptions dealing with venereal disease.
7. Stenciling of the VD story and the slogan "KO-VD" on sidewalks in the Loop and elsewhere in the city.

The use of skywriting on the opening day of the campaign to spell out the slogan "KO-VD" 50 times over the city, in conjunction with sky banners saying, "KO Syphilis, Call Randolph 6–8000," was followed within 2 hours by almost 300 telephone calls to the Health Department's "Extension VD."

VD Control Program Approved by WHO Committee

According to a recent United Nations press release, the Second World Health Assembly's Committee on Program has approved at Rome proposals for three fundamental health programs — health services for mothers and children, a world-wide training project for medical, nursing, and other public health personnel, and a plan for the control of venereal diseases.

The venereal disease control plan, approved June 17, 1949, includes initiation of venereal disease programs in underdeveloped areas and strengthening of existing national venereal disease services. Other activities would include elaboration of international health regulations against venereal disease, provision of supplies such as penicillin to countries needing them, and collaboration with the International Labor Organization to check the spread of venereal disease by maritime personnel, emigrants, and migratory workers. It also provides for special projects, such as the development of a serodiagnostic standardization program, a special demonstration of venereal disease control in a major international port, and participation in a plan for eradication of endemic syphilis in Bosnia-Herzegovina (in northern Yugoslavia).

It was pointed out that a whole series of discoveries since the war, especially of penicillin, permits an aggressive approach in the field of venereal disease control, both for prevention and for treatment of these infections.

The committee further decided, at the request of Iraq and the Dominican Republic, that WHO should set up a special expert group for the study of bejel and yaws, which are akin to venereal diseases but are nonvenereal.

All three of these health programs were approved by the Assembly in Rome in plenary session, according to the July issue of *For a Healthier World*, a publication issued by the Office of International Health Relations, United States Public Health Service.

WHO Meeting Seeks to Control VD Among Rhine River Boatmen

According to a recent United Nations press release, plans for international control of venereal disease among Rhine River boatmen and their families have been drafted at a five-nation meeting of experts under sponsorship of the World Health Organization at Geneva. The 3-day session was attended by experts from Switzerland, from France, from Belgium, from the Netherlands, and from the French, British, and American zones of Germany, as well as by two German health officers from Westphalia and Wurttemberg.

The spread of venereal disease through Rhine shipping has long been recognized as an international health threat, especially in the postwar period. Measures planned at the Geneva meeting for prevention and control of venereal infection among 80,000 Rhine boatmen and their families include:

1. Development of existing diagnostic and treatment centers in 15 principal Rhine ports.

2. Free medical examination and hospitalization for nationals and foreigners alike.

3. Distribution to patients of a treatment booklet published in French, Dutch, English, and German.

4. International tracing of infectious contacts.

5. Investigations necessary for epidemiologic action and social services to patients and families.

Similar measures were provided for in the international Brussels Agreement of 1924, but they were not applied to inland waterways. WHO is now preparing, with other interested bodies, international health regulations for venereal disease control which have been promulgated by the World Health Assembly (the legislative body of WHO) and which will be applied in sea and river ports throughout the world to replace the Brussels Agreement.

The Geneva conference also recommended creation of a WHO regional expert venereal disease commission for the Rhine area this year, with a technical medicosocial center in Rotterdam.

The conference recommendations were submitted to the WHO Executive Board in July after the World Health Assembly's session, which opened June 13.

Contact Investigations in Illinois, 1948

The results of contact investigations in 1948 by health departments in Illinois (exclusive of Chicago) were recently analyzed by Dr. Leonard M. Schuman, Chief of the Division of Venereal Disease Control, Illinois State Department of Public Health in his *Informational Bulletin of Venereal Disease Control*.

According to the analysis, contract tracing, because of its selectivity, remains one of the most important methods of new case finding. Of the total number of syphilis cases found, 25 percent were located through contact tracing. This method was highly productive in bringing to diagnosis and treatment many cases of primary and secondary syphilis, since, out of every 100 cases found by contact tracing, 39 were found to be in the highly infectious stages.

In the analysis of the investigations completed in 1948, it was reported that, of the 3,338 contacts investigated, 2,462 were examined, of whom 1,114 were infected and 1,051 were treated. A comparison of contact investigation results between 1947 and 1948 indicated a 9.1 percent decrease in the number of contacts investigated, a 10.8 percent decrease in the number examined, a 14.3 percent decrease in the number found infected, and a 13.9 percent decrease in the number treated. The reduction in the total number of investigations, according to Dr. Schuman, was largely due to the decreased number of such investigations by district and county health departments.

For all health departments, the results of contact investigations in 1948 revealed that 73.8 percent of all contacts were examined. This is an insignificant difference to the 75.1 percent examined in 1947. Dr. Schuman considered this a disappointing result considering the diminution in the number of total investigations, and he ascribed responsibility largely to the district health departments, which in 1948 presented 70.5 percent of the contacts as compared with 73.0 percent in 1947.

The analysis noted that 5.7 percent of all infected contacts were not subsequently treated. This meant that 63 contacts of the 1,114 contacts found to be infected were not placed under treatment. Both city and county health departments presented the high percentages of 7.8 and 8.7 percent, respectively, in this category.

Dr. Schuman concluded from his analysis that greater effort needs to be made in contact tracing; that more effective interviewing technics should be employed in order to elicit the naming of a greater number of contacts per case, as well as better information in order to locate the contacts so named; and that it is imperative, from the point of view of securing an accurate statistical picture of contact investigations, that every field investigation be represented by an Assignment and Report Form.

CURRENT LITERATURE

Note: Abstracts of all articles listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

Acta pharmacol. et toxicol., Copenhagen

Influence of rat liver in vivo and in perfusion experiments on penicillins F, G, K and X. K. Pedersen-Bjergaard and M. Tønnesen. 5: 13–20, Fasc. 1, 1949.

Am. J. Dis. Child., Chicago

Congenital syphilitic nephrosis successfully treated with penicillin. John P. Scully and James N. Yamazaki. 77: 652–658, May 1949.

Am. J. M. Sc., Philadelphia

* Observations on penicillin-treated cardiovascular syphilis. Joseph Edeiken, Mortimer S. Falk and Howard P. Steiger. 217: 475–484, May 1949.

Observations on penicillin-treated cardiovascular syphilis. Joseph Edeiken, Mortimer S. Falk and Howard P. Steiger. Am. J. M. Sc., 217: 475–484, May 1949.

Fifty patients with cardiovascular

syphilis who were admitted to the Institute for the Study of Venereal Disease were treated with sodium penicillin in aqueous solution in total dosages ranging from 1,200,000 to 9,600,000 Oxford units. There were 23 patients with uncomplicated aortitis, 20 with aortic insufficiency, 5 with aortic aneurysms, and 2 with both aneurysms and aortic insufficiency. The patients, of whom 28 were white and 22 Negro, ranged in age from 26 to 69 years. There were 40 male and 10 female patients.

Forty patients had received metal chemotherapy previously; however, only four had received any treatment within the 3-month period prior to the administration of penicillin.

In no instance was it necessary completely to interrupt treatment because of untoward reactions. The lack of untoward symptoms in patients with severe myocardial lesions is especially noteworthy. Two patients with probable ancient posterior infarctions experienced no adverse reaction to penicillin therapy. Five patients with aortic regurgitation and one with aortic regurgitation and aneurysm who were in marked cardiac failure were treated with penicillin at the same time measures were taken to combat congestive failure. Not only did they tolerate both treatments well, but all were markedly improved on discharge. Thus, contrary to the heretofore accepted practice of giving no potent spirocheticidal drug to decompensated cardiovascular syphilis patients, it does not seem necessary to delay penicillin treatment until compensation is restored.

There appeared to be no relationship between the amount of penicillin in the initial dose and the occurrence of a febrile Herxheimer reaction. No clear-cut case of therapeutic paradox was seen in this series of patients during the period of observation, although sufficient time has not yet elapsed to warrant drawing definite conclusions.

Twenty-eight patients had electrocardiograms at approximately 3-day intervals during the course of treatment. Electrocardiographic changes (significant T-wave changes) were noted during the course of treatment in eight patients. Thirty-four patients on whom electrocardiograms were made after treatment are still being followed.

Although prolonged observation of a larger group of cases is needed, there are indications that penicillin is of value in the treatment of syphilitic heart disease.

AM. J. MED., NEW YORK

Cerebral blood flow and oxygen consumption in neurosyphilis. John L. Patterson, Jr. and Albert Heyman. (American Federation for Clinical Research. Abstracts: Southern Sectional Meeting, New Orleans, Jan. 28, 1949.) 7: 134, July 1949.

AM. J. OBST. & GYNEC., ST. LOUIS

A study and classification of pelvic inflammatory disease. [Gonorrhea.] Roy W. Mohler. 57: 1077–1086, June 1949.

The role of penicillin in obstetrics. [V. D.] L. Marshall Harris and Daniel M. Shook. 57: 1186–1198, June 1949.

AM. J. SURG., NEW YORK

Survey of the value of neurosurgical treatment for the relief of intractable pain. [Syphilis.] Michael Scott and Henry T. Wycis. 77: 718–736, June 1949.

AM. J. SYPH., GONOR. & VEN. DIS., ST. LOUIS

Morphology, cultural characteristics, and a method for mass cultivation by the Reiter spirochete. Abraham Gelperin. 33: 101–113, Mar. 1949.

The problem of the "biologic false" or nonspecific positive serologic test for syphilis. Clinical observations and case studies. John H. Stokes and G. W. James. 33: 114–125, Mar. 1949.

*Efficacy of penicillin treatment of early syphilis in the Army. L. Altshuler, Bernard D. Karpinos, William Leifer and J. J. Ozog. 33: 126–138, Mar. 1949.

Chronic adhesive arachnoiditis. (Probably due to virus of lymphogranuloma venereum.) Frederick E. G. Valergakis, Arthur Sutherland and Herbert Koteen. 33: 139–142, Mar. 1949.

*The treatment of syphilitic primary optic atrophy with penicillin and with penicillin and malaria. S. F. Horne and Arthur C. Curtis. 33: 143–151, March. 1949.

*Experimental studies on the pathogenicity of *Donovonia gronulomatis.* Robert B. Dienst, Calvin H. Chen and Robert B. Greenblatt. 33: 152–157, Mar. 1949.

Aerorectogram as an aid in the evaluation of rectal stricture due to lymphogranuloma venereum. R. Frank Jones. 33: 158–163, Mar. 1949.

- *Evaluation of twelve media for the isolation of the gonococcus. Charles M. Carpenter, Matthew A. Bucca, T. C. Buck, E. P. Casman, C. W. Christensen, Ed Crowe, Ruth Drew, Justina Hill, Charles E. Lankford, Harry E. Morton, Lenore R. Peizer, Carolyn I. Shaw and J. D. Thayer. 33: 164–176, Mar. 1949.
- *The treatment of gonorrhea with streptomycin. S. Ross Taggart, Harold L. Hirsh, Franklin D. Hendricks, G. Roland Gable, Michael A. Puzak and Aston B. Greaves. 33: 177–179, Mar. 1949.
- The treatment of chancroid with streptomycin. S. Ross Taggart, Harold L. Hirsh, Franklin D. Hendricks, G. Roland Gable, Michael A. Puzak and Aston B. Greaves. 33: 180–181, Mar. 1949.
- Gonococcal infection of the median raphe. Robert A. Mee. 33: 182–186, Mar. 1949.
- The intent of the American Venereal Disease Association. Roger W. Barnes. 33: 187–188, Mar. 1949.

Efficacy of penicillin treatment of early syphilis in the Army. L. Altshuler, Bernard D. Karpinos, William Leifer and J. J. Ozog. Am. J. Syph., Gonor. & Ven. Dis., 33: 126–138, Mar. 1949.

This study was undertaken by the Army to determine the therapeutic efficacy of its penicillin schedule for the treatment of early syphilis which consisted of 60 intramuscular injections of 40,000 units of aqueous amorphous penicillin at 3-hour intervals, for a period of 7½ days. During the 19-month period from June 1944 to December 1945, changes occurred in the proportion of G, F, X, and K species in amorphous penicillin. In an effort to determine the influence of these changes on the therapeutic outcome, the patients were separated on the basis of the period of treatment coincident with these changes. The material for the study was obtained from the Syphilis Register in the Office of the Surgeon General of the Army and included 30,972 patients. Of these, 22,065 were observed for less than 6 months, while 8,907 patients had a follow-up of 6 months or more.

According to the criteria used for classifying the results, no patient was considered a success before the termination of at least a 6-month follow-up. Patients who developed new syphilitic lesions at any time after completion of treatment were classified as infectious relapse, disregarding the possibility of reinfection. Patients with seronegative primary syphilis were classified as serologic relapse whenever the serologic test was doubtful or positive after a 6-month follow-up. Patients with seropositive primary and secondary syphilis were not considered failures even though the serologic reactions had not become negative before the termination of the follow-up, unless the serologic reaction had been recorded at any time as doubtful or negative and subsequently as positive. Patients with seropositive primary and secondary syphilis who showed a doubtful or positive reaction after follow-up were classified as seroresistant. A doubtful or definitely abnormal spinal fluid placed the patient in the category of failure. Every patient re-treated for any reason was considered a failure.

Distribution of these patients by period of treatment, stage of infection, race, and result of classification is presented in table form. That the failure rate of early syphilis varies considerably with the stage of infection was confirmed by this study. The incidence of failure was lowest in the seronegative primary stage with a rate of 87.3 per 1,000 patients of both racial groups, higher in the seropositive primary syphilis stage with 186.2 per 1,000 patients, and highest in secondary syphilis with 282.7 per 1,000 patients. The total failure rate was 159.1 per 1,000 treated patients.

The failure rate was consistently higher among Negro patients than among white patients in each stage of infection and each period of treatment. The total failure rate for white patients was 100.5 per 1,000 treated individuals, and 227.0 per 1,000 Negro patients. The most striking increase in the failure rate occurred during the third period of treatment and was thought to be due to the change in the chemical composition of penicillin which consisted of an increase in the ineffective K species at the expense of the potent G species.

Findings indicated the beneficial effect of penicillin on abnormal spinal fluid.

Among a total of 5,600 spinal fluid examinations performed subsequent to treatment, only 3 doubtful and 21 abnormal spinal fluids were found, which seemed to indicate a remarkable neurotropic effect of penicillin.

The treatment of syphilitic primary optic atrophy with penicillin and with penicillin and malaria. S. F. Horne and Arthur C. Curtis. Am. J. Syph., Gonor. & Ven. Dis., 33: 143–151, Mar. 1949.

Only patients who satisfied all the examiners that they had syphilitic primary optic atrophy were included in this study. Of the 42 patients under study, 15 (36 percent) were treated with penicillin alone, while 27 (64 percent) were treated with penicillin and malaria. The penicillin for both groups was administered in saline, 40,000 units intramuscularly every 3 hours for 100 injections. The majority of those treated with malaria in addition to penicillin received 10 paroxysms with at least 50 hours of fever over 103.5° F. rectally, but a few received one-half that amount of fever.

Complete follow-up examinations after 2 years were done on 7 of the patients, 2 of whom were treated with penicillin alone and 5 with the combined schedule. For 4 other patients (2 treated with each schedule), who had maintained useful vision for 2 years subsequent to treatment, follow-up visual-field examinations were not possible during the second post-treatment year. Ophthalmologic examinations were impossible to obtain on 5 patients who had maintained useful vision for 2 years after termination of treatment. One of these received penicillin alone, while 4 received malaria and penicillin. The criteria for the maintenance of useful vision are based on statements from the patient and/or referring physician that the patient was able to perform satisfactorily at his usual occupation. Seven of the group have been treated too recently for analysis, and 14 have been lost to follow-up or re-treated contrary to the advice of the authors. Six patients who were blind prior to treatment showed no change in visual acuity.

From 16 patients followed for 2 years, 5 were treated with penicillin and 11 with combined therapy. There were two treatment failures among those who received malaria and penicillin and no failures in the 5 patients who received penicillin alone. From this small group of 16 patients followed for 2 years, penicillin alone appeared to be as effective as therapeutic malaria. One patient had a return to normal vision.

Experimental studies on the pathogenicity of *Donovania granulomatis*. Robert B. Dienst, Calvin H. Chen and Robert B. Greenblatt. Am. J. Syph., Gonor. & Ven. Dis., 33: 152–157, Mar. 1949.

This study was undertaken in an effort to produce experimental reproduction of granuloma inguinale with cultured forms of Donovan bodies.

The *Donovania granulomatis* cultures were obtained either from diseased tissue (G and Z strains) or from the aspirated pus of unruptured inguinal swelling (A strain) of granuloma patients. Strains A and Z were also grown on fresh yolk agar medium and both the infected embryonic yolk sac and the fresh yolk agar cultures were used in the experiments.

For the animal experiment, subcutaneous inoculations were made on a young adult female rabbit. In all instances the inoculated areas became indurated with nodule formation which persisted from 2 to 8 weeks. Smears made from these nodules 1 week after the last inoculation in each case revealed no organisms. Inoculations were also made intracerebrally in mice; intradermally and subcutaneously in mice, guinea pigs, and rabbits; into the tuberculous lymph nodes of experimentally infected guinea pigs; and into the medullary cavity of the femur of rabbits. No infection was observed in any of these animals either by tissue smears or biopsy sections.

Case histories are presented of four human experiments. In these, inoculations were given intradermally and subcutaneously. All inoculations were failures whether given as simple inoculations, inoculations on top of artificially produced chancroid lesions and lecithin-produced nodules, or when a filtrate made from fresh granuloma tissue was added to the culture before inoculation so as to provide a coinfection factor that might be present in the tissue transplants or aspirated pus.

The cause of failure in reproducing the disease with organisms remains as obscure as the mode of transmission of the disease itself. Since the cultured organisms are extracellular, it may be that the intracellular form as it occurs in diseased tissue is the infectious form.

Evaluation of twelve media for the isolation of the gonococcus. Charles M. Carpénter, Matthew A. Bucca, T. C. Buck, E. P. Casman, C. W. Christensen, Ed Crowe, Ruth Drew, Justina Hill, Charles E. Lankford, Harry E. Morton, Lenora R. Peizer, Carolyn I. Shaw and J. D. Thayer. Am. J. Syph., Gonor. & Ven. Dis., 33: 164–176, Mar. 1949.

This evaluation was undertaken to determine the most suitable medium for use in public health laboratories. The specimens for culture were obtained from the venereal disease clinics of the New York City Health Department, the Municipal Court of the City of Philadelphia, the Philadelphia General Hospital, and the Douglas Hospital at Philadelphia. Standard procedures for the collection of specimens were used with the time elapsing between collection of the specimens and their inoculation onto the medium varying from 1 hour to 13 hours and 45 minutes. A total of 209 specimens was tested on each medium.

The formulas and methods of preparation of the 12 mediums used are described and included the following: (1) Modified McLeod's agar with Nile Blue A and enriched with horse plasma and hemoglobin; (2) GC agar base, experimental, with bacto-hemoglobin and supplement B; (3) proteose No. 3 agar with Nile Blue A and enriched with horse plasma and hemoglobin; (4) proteose No. 3 agar with bacto-hemoglobin and a defined supplement; (5) GC agar base, experimental, with bacto-hemoglobin and supplement A; (6) proteose No. 3 agar with bacto-hemoglobin and supplement A; (7) casein-hydrolysate starch agar; (8) proteose No. 3 agar with bacto-hemoglobin and supplement B; (9) noninfusion blood agar; (10) proteose No. 3 agar with bacto-hemoglobin; (11) cystine-glucose chocolate agar; and (12) dehydrated casein-hydrolysate starch agar.

A total of 70 strains of gonococcus was isolated from the 209 specimens cultured on the 12 mediums. The number of strains recovered on a single medium ranged from 28 to 65. The maximum number recovered on a single medium was 65, these being isolated on a modified McLeod's agar with Nile Blue A and enriched with horse plasma and hemoglobin. With the exception of medium No. 2, either Nile Blue A or crystal violet was incorporated in all of the mediums which yielded the greatest number of strains of gonococci. The statistical significance of the data was determined by the X^2 test. It was evident that mediums Nos. 1, 2, and 3, for practical purposes, are equivalent. The advantages of medium No. 2 over 1 and 3 are its simplicity of preparation and the fact that the cultures may be examined after incubation for 24 hours.

The treatment of gonorrhea with streptomycin. S. Ross Taggart, Harold L. Hirsh, Franklin D. Hendricks, G. Roland Gable, Michael A. Puzak and Aston B. Greaves. Am. J. Syph., Gonor. & Ven. Dis., 33: 177–179, Mar. 1949.

A report of the treatment of 229 gonorrhea patients with 0.6 gm. and lesser amounts of streptomycin in water solution as a single injection in the gluteal muscle is presented. The study included 39 females and 190 males. Either three consecutive negative cultures within 10 days or two consecutive negative cultures at weekly intervals were considered evidence of cure.

Over 90 percent of the patients treated responded favorably to dosages of 0.3 to 0.6 gm. of the drug. All failures occurring on 0.3 gm. streptomycin were retreated successfully by the use of 0.6 gm. streptomycin. One failure on 0.5 gm.

streptomycin was re-treated successfully with 0.6 gm. Two patients treated with 0.1 gm. were classed as failures, but were cured by re-treatment with 300,000 units of penicillin in oil and beeswax, and another failing on 0.1 gm. of streptomycin was cured with 0.2 gm. Two failures occurring with 0.2 gm. streptomycin were cured by re-treatment with 0.2 gm. streptomycin.

Toxic reactions were mild, even though some patients complained of pain at the site of injection. No skin reactions were noted.

Because streptomycin does not inhibit the activity of the spirochete when given in doses of 0.5 gm., it quite possibly will not mask a developing case of syphilis by prolonging the incubation period or preventing the early clinical manifestations of the disease.

ARCH. DERMAT. & SYPH., CHICAGO

Prevention of syphilis. Penicillin calcium in oil and white wax, U. S. P. bismuth ethylcamphorate and oxophenarsine hydrochloride in treatment, during incubation stage, of persons exposed to syphilis. Lee J. Alexander and Arthur G. Schoch. 59 : 1–10, Jan. 1949.

*Neurosyphilis. Penicillin and malarial fever therapy versus penicillin and vaccine (typhoid) fever therapy. John B. Watson. 59 : 86–93, Jan. 1949.

Cutaneous manifestations of some tropical diseases. [Yaws and pinta.] Howard Fox. 59 : 127–144, Feb. 1949.

Reiter's syndrome with keratotic dermatitis. Report of a case. J. H. Peters. 59 : 217–229, Feb. 1949.

Neurosyphilis. Penicillin and malarial fever therapy versus penicillin and vaccine (typhoid) fever therapy.—John B. Watson. Arch. Dermat. & Syph., 59: 86–93, Jan. 1949.

Data pertaining to 15 patients treated with vaccine (typhoid) fever and penicillin, and 17 patients treated with malarial fever and penicillin, are presented. About 80 percent of the patients in each group had dementia paralytica or the tabetic form of dementia paralytica, while the remaining 20 percent had asymptomatic neurosyphilis, tabes dorsalis, or meningovascular neurosyphilis.

Both groups of patients received 100,000 units of crystalline penicillin sodium G, intramuscularly, every 3 hours for 25 days, making a total of 20,000,000 units. Effective fever as used in both groups of fever therapy was arbitrarily defined as the number of hours the patient's temperature remained at 103° F. (axillary) or over.

The technic of vaccine fever therapy, complications of vaccine fever therapy, complications of malarial fever therapy, laboratory studies, and clinical results are discussed.

Malarial fever therapy was found to be superior to vaccine therapy because of: (1) Comfort to the patient and ease of administration; (2) the percentage of patients who were improved was much greater, and the percentage who were worse was much less than in vaccine fever therapy; (3) there were fewer and less serious complications; and, (4) there were no malarial relapses after the patient was treated with 3.2 gm. of quinacrine hydrochloride over a 6-day period.

The erythrocyte count and hemoglobin determination tests were found to be useful in judging the condition of the patient in malarial fever therapy. No laboratory test was found which would aid in evaluating the condition of a patient receiving vaccine fever therapy.

Crystalline penicillin sodium G, 20,000,000 units given over a period of 25 days, seemed to be of minimal or no benefit in cases of paresis and the tabetic form of dementia paralytica. There were no deaths with either form of fever therapy.

ARKANSAS HEALTH BULL., LITTLE ROCK

Evaluation of Venereal Disease Department of Jefferson County—1941–1948. W. H. Bruce. 6 : 6, May 1949.

VD information project announced. 6 : 10, May 1949.

BRIT. M. J., LONDON

Non-specific effects of impure penicillin. J. Ungar. No. 4606 : 654–657, Apr. 16, 1949.

BULL. VEN. DIS., BOSTON

Cutaneous manifestations of late syphilis. Francis M. Thurmon. 12 : 1–6, Apr. 1949.

Maternal and congenital syphilis. Benjamin Ferris. 12 : 1–4, July 1949.

Connecticut M. J., New Haven

Some reactions to anti-biotics. Leon Goldman. 13 : 420–423, May 1949.

Delaware State M. J., Wilmington

Problems in genito-urinary diagnosis and treatment in a community hospital. [V. D.] Ervin L. Stambaugh. 21 : 87–96, June 1949.

Dis. Nerv. System, New York

Evaluation of progress in establishing physiochemical treatments in neuropsychiatry. I. The present status of the treatment of neurosyphilis. A. E. Bennett. 10 : 131–136, May 1949.

Edinburgh M. J., Edinburgh

Judgment in cardiology. [Syphilis.] Part I. Richard W. D. Turner. 56 : 1–12, Jan. 1949.

Florida Health Notes, Jacksonville

Venereal diseases. 41 : 126–127, June 1949.

Glasgow M. J., Glasgow

Diabetic neuropathy with Argyll-Robertson pupils : report on two cases. Mary D. Smith. 30 : 181–184, May 1949.

Health, Toronto

More power to public health. Part 2. [V. D.] G. D. W. Cameron. Pp. 6–7, Mar.–Apr. 1949.

Hygeia, Chicago

The "minor" venereal diseases. V. D.—Part IV. Henry Packer. 27 : 406–407, 416, June 1949.

J. A. M. A., Chicago

Prevention of gonorrhea with penicillin tablets. Harry Eagle, A. V. Gude, G. E. Beckmann, G. Mast, J. J. Sapero and J. B. Shindledecker. 140 : 940–943, July 16, 1949.

J. Invest. Dermat., Baltimore

Serum concentration following the oral administration of crystalline procaine penicillin G and crystalline sodium penicillin G. D. K. Kitchen, E. W. Thomas and C. R. Rein. Preliminary and Short Reports. 12 : 147–149, Mar. 1949.

J. M. A. Eire, Dublin

The problem of defaulters in the treatment of syphilis. P. Raymond Oliver. 24 : 72–73, May 1949.

J. M. A. Georgia, Atlanta

Oral aureomycin therapy for chancroid. Report of a case. Calvin H. Chen, Robert B. Dienst and Robert B. Greenblatt. 38 : 205–206, May 1949.

Chloromycetin in the therapy of granuloma inguinale. Robert B. Greenblatt, Virgene S. Wammock, Robert B. Dienst and Robert M. West. 38 : 206–208, May 1949.

J. Maine M. A., Portland

Antibiotic recent trends. Philip P. Thompson, Jr. 40 : 43–46, Feb. 1949.

J. Nerv. & Ment. Dis., Richmond

The infusion of fluids into the subarachnoid space of human beings. [Syphilis.] Louis Linn. 109 : 428–439, May 1949.

Management of neurosyphilis. C. Earle Johnson. 109 : 451–462, May 1949.

J. Oral Surg., Chicago

Neoplastic lesions of interest to the dental profession. [Syphilis.] Francis P. McCarthy. 7 : 208–216, July 1949.

J. Pediat., St. Louis

Observations on the use of procaine-penicillin. Merl J. Carson, Ruth B. Gerstung and Herbert A. Mazur. 34 : 40–43, Jan. 1949.

Pathologic findings in the neonatal period. [Syphilis.] James B. Arey. 34 : 44–48, Jan. 1949.

Toxicity of caronamide. Report of a case. Wendell Davis and Walter T. St. Goar. 34 : 83–86, Jan. 1949.

Studies on antibiotics in the cerebrospinal fluid. I. The inhibitory effect of normal cerebrospinal fluid on the antibacterial action of streptomycin. Robert G. Jordan, Jr. and Fontaine S. Hill. 34 : 579–582, May 1949.

J. Roy. Army M. Corps, London

Venereal disease and the West African in London. R. R. Willcox. 92 : 168–172, Apr. 1949.

J. Roy. Nav. M. Serv., London

Venereal disease in the West Indies. Basil Geoghegan. 35 : 94–96, Apr. 1949.

J. Urol., Baltimore

Hyaluronidase concentration in the semen as a test for patency of the vasoepididymal ducts. [Gonorrhea.] Lewis Michelson and Peter Koets. 61 : 803–805, Apr. 1949.

M. Ann. District of Columbia, Washington

The clinical use of aureomycin. Emanuel son and Peter Koets. 61 : 803–805, Apr. 1949.

Aureomycin in various infections : report of one hundred eighty cases and review of the clinical literature. Harry F. Dowling, Mark H. Lepper, Esten R. Caldwell, Richard L. Whelton and Lewis K. Sweet. 18 : 335–344, 382, July 1949.

M. Press, London

Common skin affections in childhood. [Syphilis.] John T. Ingram. No. 5738 : 397–400, Apr. 27, 1949.

Chronic valvular disease of the heart. [Syphilis.] C. T. Andrews. Modern

Treatment In General Practice. Sixteenth Series—Article No. 16. No. 5741: 473–476, May 18, 1949.

A modern survey of alopecia areata and its treatment. [Syphilis.] Allan Bigham. No. 5742: 497–500, May 25, 1949.

Psychiatric reflections. [Syphilis.] Harvey Baird. No. 5743: 527–531, June 1, 1949.

MISSISSIPPI DOCTOR, BOONEVILLE

Preventable disease control—January 1–June 30, 1949. [V. D.] A. L. Gray. 27: 81–83, July 1949.

MISSISSIPPI VALLEY M. J., QUINCY

On the use of drugs in cardiovascular disease. [Syphilis.] Julius Jensen. 71: 53–56, Mar. 1949.

NATURE, LONDON

Chloromycetin: its structure and synthesis. H. Raistrick. No. 4145: 553–554, Apr. 9, 1949.

NEW ENGLAND J. MED., BOSTON

A medical survey of the Aleutian Islands (1948). [V. D.] Fred Alexander. 240: 1035–1040, June 30, 1949.

Preventive medicine. [V. D.] Miriam D. Manning. Medical Progress. 240: 1047–1053, June 30, 1949.

Fatal Jarisch-Herxheimer reaction with sudden aneurysmal dilatation and complete bronchial occlusion following penicillin therapy. William C. L.Diefenbach. 241: 95–96, July 21, 1949.

PROC. STAFF MEET., MAYO CLINIC., ROCHESTER

*Aureomycin: studies on absorptiton, diffusion and excretion. Wallace E. Herrell and Fordyce R. Heilman. 24: 157–166, Mar. 30, 1949.

*The oral use of aureomycin in the treatment of late cutaneous syphilis. Paul A. O'Leary, Robert R. Kierland and Wallace E. Herrell. 24: 302–306, May **25, 1949.**

Aureomycin: studies on absorption, diffusion and excretion. Wallace E. Herrell and Fordyce R. Heilman. Proc. Staff Meet., Mayo Clin., 24: 157–166, Mar. 30, 1949.

The authors present a report on their studies of the absorption, diffusion, and excretion of aureomycin in human beings. The studies were based on the procedure for the assay of aureomycin in various body fluids which is used in the laboratories of the Mayo Clinic. This procedure is described in detail. Aureomycin was administered to a number of patients in amounts which were regarded as therapeutically effective.

It was found that aureomycin is readily absorbed into the general circulation. Following the oral administration of single doses of 0.75 to 1 gm. the serum content of aureomycin rapidly approaches therapeutic levels and in some instances is maintained at a rather constant level for a number of hours. Complete disappearance of all activity from the serum may not occur for 24 to 30 hours. These findings seem to confirm the fact that aureomycin is excreted rather slowly, and antibiotic activity remains in the blood considerably longer than has been the case with most previously available antibiotic substances. When 0.75 to 1 gm. of aureomycin is administered orally every 6 to 8 hours, the serum content of aureomycin varies between 2, 4, and sometimes 8 μg. per milliliter. Repeated and prolonged administration does not result in concentrations higher than 8 μg. per milliliter. This suggests that there is no "piling up" effect following multiple doses (provided that there is no impairment of renal function). No attempt has been made in these studies to find the maximal or minimal effective therapeutic dose.

These studies indicate that aureomycin is absorbed and distributed in many body fluids and tissues. Following its absorption it diffuses readily into the cerebrospinal fluid in amounts which might be considered therapeutically effective. Also, aureomycin diffuses through the placenta and is available in the fetal circulation. Inasmuch as this antibiotic has been found to be effective in the treatment of syphilis, these findings may be of some value if aureomycin finds wide use in syphilis therapy.

When therapeutically effective amounts of aureomycin are present in the serum, diffusion occurs into the pleural fluid. Aureomycin appears to be concentrated in the normal hepatic system and is excreted in the bile. Large amounts are constantly excreted in the urine. Aureomycin has been found in the liver, kidney, spleen, and lung, also.

The authors conclude with the hope that these studies will prove of some value in the outline of treatment and the interpretation of results which might be obtained after the use of aureomycin in the treatment of the variety of infections owing to organisms susceptible to its action.

The oral use of aureomycin in the treatment of late cutaneous syphilis. Paul A. O'Leary, Robert R. Kierland and Wallace E. Herrell. Proc. Staff Meet., Mayo Clin., 24: 302–306, May 25, 1949.

Previous reports have shown that aureomycin administered orally brought about the disappearance of the *Treponema pallidum* and that weight for weight it is two to three times as effective as penicillin in treating relapsing fever and leptospirosis icterohaemorrhagica.

The authors report two patients with late nodulo-ulcerative lesions of syphilis who were successfully treated with oral aureomycin.

The first patient's serologic tests were positive with a normal cerebrospinal fluid. He received 250 mg. of aureomycin orally every 6 hours for 3 days. The dose was then increased to 500 mg. every 6 hours for 3 days. On the seventh day 750 mg. every 6 hours for 2 days were administered. Finally, 1 gm. every 6 hours was given until a total of 56.5 gm. was reached for a complete treatment.

By the fifth day rapid resolution of the syphiloderms was observed. Sixty-nine days after initiating treatment, the patient returned and was observed to be clear of lesions. Though the serologic reactions were still positive, the Kahn titer dropped from 128 units to 64 units.

The second patient showed a positive serologic test, a Kahn titer of 256 units, and a normal cerebrospinal fluid. He received 250 mg. of aureomycin by mouth every 6 hours for 2 days at which time involution of the lesions was observed. The dose was increased to 1 gm. every 6 hours for 5 days. The appearance of toxic reactions forced a reduction to 500 mg. every 6 hours until a total of 60 gm. had been administered as therapy. Rapid resolution and healing resulted from this therapy.

More observations on cases of acute and chronic syphilis should be made in order to determine better dosage, duration of treatment, complications, and effects of concurrent use of aureomycin and penicillin.

Work is now being done on patients with neurosyphilis. To date the changes in the cerebrospinal fluid are serologically the same for both aureomycin and intramuscular penicillin. Unlike penicillin, aureomycin has been demonstrated in the spinal fluid of several patients.

Oral aureomycin therapy is favored over intramuscular penicillin for the following reasons: (1) Pills are more favored by patients than intramuscular injections; (2) the hazard of self-medication exists in either therapy; (3) many do not complete the short penicillin courses; (4) statistics on oral therapy will for a time be inconclusive until an evaluation of the clinical and serologic status is determined; (5) more will be able to complete the therapy due to the mild toxic reactions; (6) the treatment load will be lessened in the clinics and more man hours will be gained by industry; and (7) it is a practical and economical method of treating certain types of syphilis.

This drug may fill the need for a new antibiotic agent in the treatment of syphilis. It may be used in penicillin-resistant conditions and in penicillin-sensitive cases.

TROP. DIS. BULL., LONDON

The bone lesions of yaws in Uganda. A clinical and radiological study. C. J. Hackett. 46: 472–476, May 1949. [Abstract of thesis presented to the University of London for the Ph. D. degree, November, 1947.]

WORLD HEALTH ORGAN. NEWSLETT., GENEVA

The WHO programme and budget estimates for 1950. Venereal Diseases. No. 6: 4, Apr. 1949.

Tackling venereal diseases on inland waterways: control project on the Rhine. No. 7: 1, May 1949.

Children's health activities develop. Against syphilis and malaria. No. 7: 4, May 1949.

Second World Health Assembly opens on June 13. The job to be done. Venereal diseases. No. 8: 1–4, June 1949.

STATISTICS

Cases of Syphilis and Gonorrhea Reported to the Public Health Service by State and Territorial Health Departments, January–March 1949

[Known military cases excluded]

Area	Syphilis															Gonorrhea		
	Primary and secondary			Early latent			Late and late latent			Congenital			Not stated					
	Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter		Total all sources	Ratio to prior quarter	
		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources		All sources	Private physician sources
Region 1—Total	283	0.87	0.92	200	1.16	1.03	615	1.03	0.86	66	1.05	1.03	118	0.91	1.00	980	0.86	0.86
Connecticut	44	.76	.68	44	.67	.64	106	.85	.76	9	(*)	(*)	45	.92	(*)	205	.88	.93
Maine	72	.97	.92	24	(*)	(*)	41	.66	.42	9	(*)	(*)	1	(*)	(*)	69	.84	.75
Massachusetts	111	.88	1.11	82	1.67	(*)	321	1.21	.99	29	.85	(*)	0	–	–	568	.88	.91
New Hampshire	24	(*)	(*)	8	(*)	(*)	25	.76	.71	2	(*)	(*)	2	(*)	(*)	29	.69	.64
Rhode Island	17	(*)	(*)	35	(*)	(*)	108	1.10	1.06	12	(*)	(*)	50	1.28	(*)	77	1.10	1.65
Vermont	15	(*)	(*)	7	(*)	(*)	14	(*)	(*)	5	(*)	(*)	20	.59	.59	32	.49	.49
Region 2—Total	1,712	.85	.75	3,274	.94	.81	6,584	1.01	.93	345	1.00	.86	212	1.01	.89	10,028	.89	.65
Delaware	56	.97	.71	97	1.35	.86	76	1.33	(*)	8	(*)	(*)	41	.72	.27	52	1.18	(*)
New Jersey	271	1.09	1.03	694	1.11	.84	1,195	1.32	1.16	68	1.62	(*)	38	.88	(*)	1,122	.97	.71
New York	842	.70	.61	1,278	.81	.71	4,119	.93	.86	147	.77	.69	89	1.29	(*)	6,087	.79	.64
New York City	675	.68	.55	1,165	.79	.69	3,168	.93	.85	108	.81	.74	76	1.36	(*)	5,109	.83	.81
Pennsylvania	543	1.08	1.46	1,205	1.01	1.29	1,194	1.03	1.09	122	1.14	(*)	44	1.10	(*)	2,767	1.15	–
Philadelphia [a]	201	.90	–	821	1.02	–	591	.87	–	40	1.11	–	2	(*)	–	2,333	1.23	–
Pittsburgh [a]	92	.80	–	107	1.07	–	146	.94	–	20	(*)	–	0	–	–	235	.70	–
Region 3—Total	1,859	.92	.86	2,484	1.04	.83	2,441	1.11	.87	321	1.26	.84	75	1.21	(*)	12,568	.92	.70
District of Columbia	194	.77	(*)	236	.81	.61	355	.94	.94	25	.81	(*)	5	–	–	3,625	.86	.57
Maryland	446	.97	1.24	493	1.06	1.41	885	1.40	.85	60	.86	(*)	38	1.19	(*)	1,711	.98	.83
Baltimore	278	1.07	(*)	320	1.17	(*)	689	1.56	.88	37	.95	–	37	(*)	(*)	1,380	1.04	1.09
North Carolina	616	1.10	(*)	844	1.22	.80	347	1.23	.69	114	1.61	(*)	0	–	–	3,636	.96	.91
Virginia	347	.86	.73	595	1.03	.77	421	.96	.89	49	1.17	(*)	32	1.07	(*)	2,499	.90	.80
West Virginia	256	.75	.74	316	.86	.85	433	.93	.89	73	1.78	(*)	0	–	–	1,097	.98	.88
Region 4—Total	1,192	.85	.82	2,423	.97	.88	3,995	.94	.90	330	.98	.90	215	.81	.85	6,114	.88	.75
Kentucky	262	1.11	1.06	338	1.11	1.01	566	1.15	1.13	41	.93	(*)	11	(*)	(*)	1,410	.97	1.01
Michigan	374	.77	.90	578	1.08	.94	1,060	.85	.86	92	.75	1.06	204	.80	.87	2,047	.89	.88
Ohio	556	.81	.72	1,507	.91	.85	2,369	.94	.89	197	1.15	.83	0	–	–	2,657	.82	.62
Region 5—Total	1,144	.87	.86	1,701	.99	.97	2,850	.99	.96	238	.93	.79	1	(*)	(*)	7,289	.90	.79
Illinois	770	.90	.88	1,154	.97	.96	1,783	.94	.90	118	1.03	.94	0	–	–	6,247	.92	.84
Chicago	477	.87	.88	820	.97	.98	931	.88	.85	62	.93	(*)	0	–	–	4,918	.93	.91
Indiana	281	.83	.86	414	1.02	.96	621	.94	.95	89	.75	.63	0	–	–	673	.88	.86
Minnesota	22	.59	(*)	33	1.00	(*)	211	1.82	1.24	10	(*)	(*)	1	(*)	(*)	188	.61	.45
Wisconsin	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	21	(*)	(*)	0	–	–	181	.83	.67

Region 6—Total	3,295	.90	.78	6,040	1.04	.78	5,387	1.10	.75	1,176	1.03	.69	684	.83	.81	21,000	1.00	1.93
Alabama	457	.80	.89	672	.95	.83	235	.52	.58	63	1.02	(*)	640	.83	.81	1,309	1.06	.99
Florida	661	.69	.66	1,348	.92	.73	1,271	.80	.61	99	.58	.42	0	-	-	3,734	.90	.74
Georgia	725	1.05	.85	1,073	1.27	-	1,056	1.32	.75	319	1.19	-	13	(*)	-	3,765	1.07	.06
Mississippi	547	1.11	1.70	846	1.14	.72	1,702	1.77	2.24	270	1.85	(*)	0	-	-	2,432	1.05	.94
South Carolina	366	.77	.18	731	1.03	.36	343	1.06	.52	69	1.35	-	0	-	-	2,332	1.01	(*)
Tennessee	399	1.15	1.22	612	1.27	1.08	443	1.00	.87	48	.77	(*)	15	(*)	(*)	5,208	.98	7.65
Puerto Rico	135	1.05	-	748	.92	-	324	1.01	-	305	.80	-	12	(*)	-	2,175	1.03	-
Virgin Islands	5	(*)	-	10	(*)	-	13	(*)	-	3	(*)	-	4	(*)	-	45	1.15	-
Region 7—Total	612	.86	.92	874	.96	.87	1,496	.99	.98	134	1.00	1.12	157	1.15	1.13	2,065	.86	.69
Iowa	97	.76	.73	119	1.20	1.30	231	1.38	1.36	16	(*)	(*)	0	-	-	204	.79	.70
Kansas	121	.78	.81	145	.70	.64	384	.68	.66	52	1.06	(*)	27	-	-	337	1.03	.70
Missouri	297	.91	1.05	479	.96	.83	691	1.08	1.06	52	.95	(*)	67	.96	1.04	1,207	.83	.72
St. Louis	121	.88	.88	279	.96	.83	377	1.09	.97	21	(*)	(*)	0	-	-	746	.83	.70
Nebraska	49	1.40	(*)	74	1.30	1.08	143	1.44	1.39	9	(*)	(*)	52	1.02	1.04	204	1.01	.88
North Dakota	20	(*)	(*)	5	(*)	(*)	20	(*)	(*)	2	(*)	(*)	5	(*)	(*)	24	.34	.34
South Dakota	28	.64	(*)	52	1.49	(*)	27	(*)	(*)	3	(*)	(*)	6	-	-	89	.91	.71
Region 8—Total	1,680	.91	1.01	3,449	1.25	1.05	4,131	1.18	.92	1,150	1.58	.84	1,782	1.11	1.15	12,173	1.05	.94
Arkansas	315	1.14	1.16	825	1.32	1.05	1,692	1.19	.91	364	1.31	(*)	10	(*)	(*)	1,168	1.09	.68
Louisiana	385	.87	(*)	863	1.49	(*)	1,009	1.66	.48	198	2.11	(*)	360	.97	1.15	3,026	1.17	.46
New Mexico	68	1.05	(*)	141	1.19	(*)	118	1.05	(*)	22	(*)	(*)	0	-	-	195	.75	.87
Oklahoma	197	.75	.72	269	.87	.99	451	.87	.87	52	.95	(*)	34	.71	.84	1,397	.91	.87
Texas	715	.90	.95	1,351	1.19	.92	861	1.02	1.14	514	1.84	(*)	1,378	1.16	1.16	6,387	1.03	.98
Region 9—Total	113	.66	.60	160	.91	.95	302	1.03	1.03	43	1.05	(*)	12	(*)	(*)	548	.71	.57
Colorado	55	.76	.67	68	1.01	.97	126	1.20	1.30	17	(*)	(*)	0	-	-	347	.74	.57
Idaho	16	(*)	(*)	23	(*)	(*)	25	.66	(*)	5	(*)	-	7	(*)	(*)	55	.55	(*)
Montana	15	.35	.29	31	.72	(*)	62	1.19	1.12	3	(*)	(*)	1	-	-	49	.96	(*)
Utah	16	.53	(*)	21	.64	(*)	80	1.08	.91	15	(*)	(*)	0	-	-	73	.72	(*)
Wyoming	11	(*)	(*)	17	(*)	(*)	9	(*)	(*)	3	-	-	4	(*)	(*)	24	.45	.40
Region 10—Total	1,075	1.01	.93	1,302	1.13	1.08	2,807	1.18	1.06	212	1.10	1.08	205	.77	.89	7,425	.92	.76
Arizona	144	1.92	(*)	119	1.20	(*)	117	1.36	(*)	9	(*)	(*)	0	-	-	224	1.03	.97
California	755	.94	.93	974	1.20	1.13	2,155	1.18	1.02	168	1.29	1.51	153	.73	(*)	6,076	.96	.74
Nevada	31	(*)	(*)	22	.63	(*)	116	1.05	.81	11	(*)	(*)	0	-	-	136	.57	.72
Oregon	49	.86	(*)	52	1.11	(*)	90	1.08	(*)	8	(*)	(*)	0	-	-	181	.64	.39
Washington	81	.98	(*)	96	.96	(*)	204	1.05	1.12	4	(*)	(*)	15	.44	(*)	523	.72	.73
Alaska	12	(*)	(*)	23	.55	.55	39	1.03	1.03	2	(*)	(*)	36	(*)	(*)	118	.91	.91
Hawaii	3	(*)	(*)	16	(*)	(*)	86	2.39	(*)	10	(*)	(*)	1	(*)	(*)	167	.93	1.01
Canal Zone	8	(*)	-	35	(*)	-	28	(*)	-	1	(*)	-	0	(*)	-	151	.94	-
Continental United States	12,810	.89	.84	21,110	1.05	.88	30,146	1.05	.91	3,695	1.19	.91	3,408	.98	1.01	77,685	.94	.90
Total United States including Territories	12,973	.89	.84	21,942	1.04	.88	30,636	1.05	.92	4,016	1.15	.90	3,461	.98	1.01	80,341	.94	.90

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[a] From VM-820.

* Rate not calculated when base is less than 30.
– Rate not calculable. Base is zero or unknown.

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DOCUMENTS

The JOURNAL of VENEREAL DISEASE INFORMATION

Volume 30 November 1949 Number 11

ORIGINAL ARTICLES

Treponemal Immobilization Test of Normal and Syphilitic Serums . 309
Harold J. Magnuson, *Senior Surgeon*
Frederick A. Thompson, Jr., *Senior Assistant Surgeon*

Penicillin in the Treatment of Early Syphilis: 639 Patients Treated with 2,400,000 Units of Sodium Penicillin in 7½ Days 321
Herman N. Bundesen, M. D.
Frederick Plotke, M. D., M. P. H.
George X. Schwemlein, M. D.
Jack Rodriguez, M. D.

The Effect of Temperature Variants on Quantitative Turbidimetric Determinations of Spinal Fluid Protein, Using Trichloracetic Acid . 325
Virginia L. Harding, *Serologist*
Ad Harris, *Senior Serologist*

CURRENT NOTES AND REPORTS 327

CURRENT LITERATURE 329

STATISTICS

First Admissions to Mental Hospitals for All Psychoses and for Psychoses Due to Syphilis, United States, 1922, 1933–47 337

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Treponemal Immobilization Test of Normal and Syphilitic Serums[1]

Harold J. Magnuson, Senior Surgeon, and Frederick A. Thompson, Jr., Senior Assistant Surgeon,[2] United States Public Health Service

The presence of spirocheticidal substances, presumably antibodies, in the serums of patients and animals with syphilis has been demonstrated by a succession of investigators since the work of Eberson (*1*) 28 years ago. The precision and sensitivity of the technics have improved (*2*, *3*, *4*, *5*), but, until the recent work of Nelson and Mayer (*6*), all have depended in varying degree upon the in vivo demonstration of a spirocheticidal effect. Since an in vitro measure of activity would afford considerable advantage in the demonstration and study of these antibodies, it was our purpose to confirm, insofar as possible, the findings of Nelson and Mayer; to determine the precision of their technic on a large number of serums from both normal and syphilitic patients and animals; and to determine degrees to which the method might be modified to permit more convenient assays.

Methods and Materials

Blood specimens were obtained aseptically from patients with early syphilis at the Eastern Medical Center, Durham, N. C., and the Western Medical Center, Charlotte, N. C.[3] Additional specimens from patients with late syphilis and from patients with diseases other than syphilis were obtained at Duke University Hospital, Durham, N. C. Normal donors were selected from laboratory personnel and students at the University of North Carolina. The specimens from normal and syphilitic rabbits were obtained from animals under experiment in this laboratory. The serum was removed aseptically and, if not assayed immediately, was stored at —20° C. Complement, obtained in pools from at least 12 guinea pigs, was lyophilized in amounts from 3 to 5 cc., stored in vacuo at —20° C., and restored by the addition of distilled water just prior to use.

All glassware, with the exception of the fritted glass filters, was cleaned with chromic acid cleaning solution, thoroughly rinsed in both tap and distilled water, and sterilized before use. The fritted glass filters were cleaned with concentrated sulfuric acid and potassium nitrate, followed by thorough washing with distilled water until the filtrate was acid-free.

To prepare the emulsion containing *Treponema pallidum*, rabbits with an early acute orchitis were exsanguinated from the heart while receiving an infusion of isotonic salt solution in the marginal ear vein. This infusion technic was found to aid the exsanguination, permitting as much as from 200 to 400 cc. of diluted blood to be obtained by cardiac puncture instead of the usual 100 to 150 cc. obtained when saline was not given. The testes were removed aseptically, placed in a sterile egg slicer, and cut into 10 equal sections with a sterile razor blade. These were rinsed with cold salt solution and placed in a 250-cc. round-bottomed flask containing 17 cc. of Nelson's medium per testis, which medium had previously been equilibrated with 5 percent CO_2 and 95 percent N_2. The flask was thrice evacuated and filled with 5 percent CO_2 and 95 percent N_2. The spirochetes were extracted by gentle rocking in a water bath at 30° C. for a 2- to 4-hour period. Prior to use, the emulsion was filtered through a sterile, medium-porosity Corning fritted glass filter, which removed most of the red cells, gross tissue particles, spermatozoa, and from 25 to 50 percent of the spirochetes.

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[1] From the Syphilis Experimental Laboratory, U. S. Public Health Service, University of North Carolina School of Public Health, Chapel Hill, N. C. Senior Surgeon Harold J. Magnuson, Medical Officer in Charge. Aided in part by a Research Grant of the Research Grants Division, National Institutes of Health, U. S. Public Health Service.

[2] With the assistance of Mary Joy McGinn and John W. Clark, Jr., Medical Technicians.

[3] The authors are grateful to Senior Surgeon Fred W. Harb and his associates and to the Department of Medicine, Duke University, for making these serums available.

At first, the assays were performed with the volumes advocated by Nelson and Mayer (*6*) ; that is, 1.7 cc. of the filtered emulsion, 0.2 cc. of the inactivated serum to be tested, and 0.1 cc. of whole complement were added to a 25 x 100 mm. test tube. Since but a drop of the material from each tube was required for final reading of the assay, this technic represented a large waste of scarce materials, which, as will be shown below, could be remedied by the use of smaller volumes in Wassermann tubes without affecting the results of the test. The technic finally adopted consisted of inactivating a sample of the serum to be tested at 56° C. for one-half hour, placing 0.05 cc. of the serum in the bottom of a Wassermann tube (13 x 100 mm.), adding 0.1 cc. of complement diluted 1 : 4 in Nelson's medium, and finally adding 0.3 cc. of the spirochetal emulsion. A similar control tube for each serum contained the same quantities of reagents, except that the complement was heat-inactivated. Because plugs of varying tightness in the Wassermann tubes caused gassing irregularities leading to erratic survival, it was found advisable to remove the cotton plugs from all tubes just as the tubes were being placed in the anaerobe jar. If the Brewer anaerobe jar was clean, contamination of the emulsion practically never occurred. The jars containing the assay were thrice evacuated and filled with 5 percent CO_2 and 95 percent N_2.

Assays were incubated for 16 hours at 35° C. in accordance with the recommendations of Nelson and Mayer (*6*) and with the findings indicated below in the text. At the end of the incubation period, test tubes were removed from the Brewer jar and placed in random order in a test tube rack. Two or three platinum loopfuls were placed on a slide under a 22 x 22 mm. cover slip, and the percentage of motile organisms in the first 25 spirochetes was calculated. It should be noted that the specimens were read at random and that the persons making the counts had no knowledge of what the slides represented.

At first, 50 spirochetes were enumerated. but, for reasons indicated below, the majority of the assays are based upon samples of 25 spirochetes. For reasons that will be indicated in the text, the result of the immobilization test was considered positive if the percentage of motile organisms in the assay tube containing serum and active complement was at least 40 percent below that of the control tube containing the same serum and an equal amount of heat-inactivated complement. Where the difference was between 30 percent and 40 percent, the result was considered doubtful, and differences less than 30 percent were considered negative. For the purposes of this paper, the result was considered nonspecific when less than 50 percent of the organisms in both tubes or in the inactive-complement tube were living.

Since anticomplementary antigen emulsion or anticomplementary serum may give false-negative results, it is advisable to check negative reactions for the presence of residual complement at the end of the assay by adding sensitized sheep cells. This control alone will not suffice, since emulsions are occasionally encountered that give apparent positive results with normal serums. It has been our practice to include titrations of known positive and negative serums in each assay and to discard the assay unless the results with these serums are in accord with previous assays.

The Cohn fractions of normal and syphilitic human serums and normal and syphilitic rabbit serums were prepared in this laboratory by method VI of Cohn (*7*). The euglobulin fractions of serums were prepared by the method of Erickson (*8*). The VDRL cardiolipin flocculation titers and the Kahn titers were performed at either the Eastern or the Western Medical Center.

Results

A. *Comparison of the 2-cc. Volumes Employed by Nelson and Mayer With the 0.45-cc. Volumes Here Employed*

Table 1 shows the results of two titered assays performed in duplicate: (1) with the original method of Nelson and Mayer, using a volume of 2.0 cc. (*6*); and (2) with the method described above, using a final volume of 0.45 cc. in a Wassermann tube. Shown in the table are the percentages of motile organisms for the various serum dilutions in the presence and absence of active complement. It is apparent that the two technics give comparable results. Since only 0.3 cc. of emulsion is required per tube as compared with 1.7 cc. of emulsion per tube by the Nelson and Mayer (*6*) technic, the use of the smaller volume permits more than a fivefold increase in the number of serums that may be assayed with the same amount of material.

Similar studies have been made with respect to the survival of the organisms over longer periods of time and at other temperatures. Provided only that the fluid has adequate access to the 5 percent CO_2 and 95 percent N_2 and that the tubes are protected from evaporation, survival bears no relation either to the tube size or to the volume of fluid. It may be noted in table 1 that Nelson's medium alone failed to support survival of the *T. pallidum*. Serum appeared to have a beneficial effect. This is a frequent finding.

B. *Results on Normal Serums and Criteria for Abnormality*

Summarized in table 2 are 107 observations on 73 normal human serums and 103 observations on 91 normal rabbit serums. These observations extend over a 4-month period and indicate the degree of variation that may be expected in normal serums, representing the sum of the variations due to the serums themselves and those due to technic. The mean percentage survival in the normal human serums in the presence of heated complement was 89.48 percent, with a standard

Table 1.—*Comparison of large (2 cc.) versus small (0.45 cc.) volumes in the demonstration of immobilizing antibodies against* Treponema pallidum

[Shown are 2 separate assays in which titrations on syphilitic and normal serums were run simultaneously: (1) By the technic of Nelson and Mayer using 1.7 cc. of emulsion, 0.1 cc. of whole complement, and 0.2 cc. of inactivated serum; and (2) by the present technic, using 0.3 cc. of emulsion, 0.1 cc. of 1:4 complement, and 0.05 cc. of inactivated serum. The numbers in the body of the table represent the percentage of motile *T. pallidum* after 16 hours of incubation at 35° C.]

Serum	Dilution	Assay 1				Assay 2			
		Large volume		Small volume		Large volume		Small volume	
		Active complement	Heated complement	Active complement	Heated complement	Active complement	Heated complement	Active complement	Heated complement
Normal serum	1:10	96	96	92	88	88	92	96	96
	1:50	100	100	96	80	88	92	100	100
	1:250	88	100	92	96	96	92	92	92
	1:1,250	96	88	80	96	100	92	80	80
Syphilitic serum	1:10	12	92	0	100	0	96	0	100
	1:50	12	100	0	96	20	92	0	92
	1:250	84	88	76	92	56	92	16	92
	1:1,250	72	92	84	96	96	84	88	96
Filtrate	--------	84	96	88	96	96	84	92	88
Filtrate alone (no complement added)	--------	--------	20	--------	52	--------	64	--------	100

Table 2.—*Summary of immobilization assays on normal serums*

[Summarized are the results of 107 observations on 73 normal human serums and 103 observations on 91 normal rabbit serums. All assays were incubated for 16 hours at 35° C., and the percentage survival in individual assays was based on a sample of 25 spirochetes.]

	Normal human serum			Normal rabbit serum		
	Active complement	Heated complement	Mean difference	Active complement	Heated complement	Mean difference
Mean percentage motile	83.16	89.48	6.32	79.26	89.06	9.80
Standard deviation	9.41	8.26	10.60	10.81	9.24	14.40
Standard error of mean	0.9097	0.7986	----------	----------	----------	1.419
Estimated percentage false-positive if 25 counted and difference of 40 percent considered positive.	0.07			1.8		
Estimated percentage false-positive if 50 counted and difference of 25 percent considered positive.	0.64			6.7		

deviation of 8.3 percent. The mean survival in the normal serums with active complement was 83.16 percent, with a standard deviation of 9.42 percent. The difference of the two means of 6.32 percent is statistically significant (t=5.21). On the basis of the observed mean, one may calculate the theoretical sampling variation that would be encountered in counting samples of 25 spirochetes

$$\sigma=\sqrt{\frac{pq}{n}}.$$

In the case of the normal serums with inactive complement, this theoretical sampling variation equals 6.1 percent. The observed standard deviation of 8.30 is thus 1.36 times the theoretical sampling variation had all of these specimens been identical, and it may be assumed that this additional variation represents variation in the individual serums and in other undetermined variables. For the serums with active complement, the theoretical standard deviation is 7.5 percent and the observed is 9.42 percent, or the observed is 1.25 times the theoretical, this again being attributable to variations in serums.

The variation encountered among rabbit serums was somewhat greater. Whether the added variance may be ascribed in part to previous exposure of the host to *Treponema cuniculi* remains to be determined.

These data provide a base line in determining what should constitute abnormal variation between the tubes containing active complement and inactive complement. Since normal serum tested in the presence of complement gave significantly poorer survival than it did in the presence of heated complement, a proportion of any observed difference must be ascribed to this difference. If we accept a difference of 40 percent as significant, the counting of 25 spirochetes in both the control and the assay tube should result in a false-positive result due to sampling errors in approximately 1 human serum out of 1,000.[4] If 50 spirochetes are counted in each tube and differences of 25 percent or more are accepted as abnormal, as has been suggested, sampling variation should account for false-positives in approximately 1 human serum out of 160. The margin here selected as the upper limit of normality thus provides an adequate margin of safety. While the sampling error may be decreased by $\sqrt{2}$ through counting 50 rather than 25 spirochetes, in our opinion the gain is insufficient to justify the increased time involved. On theoretical grounds, it would be preferable to find the dilution of serum that would cause 50-percent killing within a given observation period, but the present cumbersome technic precludes such measurement for this survey.

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[4] $t=\frac{\text{arbitrary difference}-\text{observed mean difference}}{\text{standard deviation of mean difference}}=\frac{40\%-6.32\%}{10.61\%}=3.17.$

C. *Concentration of Complement for the Demonstration of Immobilizing Activity*

Table 3 shows the result of a typical experiment in which both normal and syphilitic serums are titered against varying amounts of guinea pig serum. It is evident that the sensitivity of the test is dependent in a large measure upon the amount of complement present and that the optimum amounts of complement are far in excess of those required for conventional complement-fixation tests. One-tenth cubic centimeter of 1 : 4 complement diluted in Nelson's medium is about the minimum that can be used in the final 0.45-cc. volume. This represents a final concentration of 1 : 18 of complement. Larger amounts of complement appear to do no harm, but are unnecessary. It has been our practice to test each new lot of complement by titration similar to this, but the guinea pigs contributing to the pool are not pretested individually.

In spite of the relatively large amounts of complement required for optimum demonstration of the immobilizing antibodies, the amount of complement fixed by the spirochetal antigen could not be measured by the usual hemolytic system technics.

D. *Time Required for Immobilization of* T. pallidum *by Syphilitic Serum*

Figure 1 shows the results of a typical assay measuring the time required for the in vitro immobilization of *T. pallidum* by syphilitic serum in the presence of active complement. The assay was incubated at 35° C. under 5 percent CO_2 and 95 percent N_2. While slight activity in the highest concentration of serum may be demonstrable in 6 hours, the effect was not definite until the 12-hour interval. As the time of exposure increased, more dilute concentrations of serum showed activity. Unfortunately, after 24 hours the normal serum controls not infrequently become erratic in their survival, making it inadvisable to continue the usual assay beyond this period. As the 18-hour interval represents a most convenient time

Table 3.—***The effect of the concentration of complement on the immobilization test***

Shown is a typical assay in which normal and syphilitic human serums were titered against varying concentrations of complement and heat-inactivated complement. Each tube contained 0.05 cc. of the dilution of human serum, 0.1 cc. of the dilution of complement, and 0.3 cc. of emulsion containing *T. pallidum*. All dilutions were made in Nelson's medium. The numbers in the body of the table represent the percentage of motile *T. pallidum* (50 organisms counted) after 16 hours' incubation at 35° C.]

	Final concentration	Active complement					Heat-inactivated complement				
		1:9	1:18	1:36	1:72	0	1:9	1:18	1:36	1:72	0
Final concentration of normal human serum.	1/10	98	84	100	90	100	84	98	94	94	100
	1/40	98	98	96	84	100	96	98	94	96	96
	1/160	88	88	98	98	98	98	98	90	84	92
	1/640	86	98	94	98	96	98	98	88	94	98
	0	96	92	80	82	80	88	96	98	94	80
Final concentration of syphilitic human serum.	1/10	0	0	10	22	80	76	74	64	88	92
	1/40	0	10	42	82	88	92	100	92	0	92
	1/160	48	38	78	96	98	96	94	92	100	96
	1/640	82	88	76	84	86	94	100	88	88	96
	0	100	88	94	90	86	98	92	94	98	84

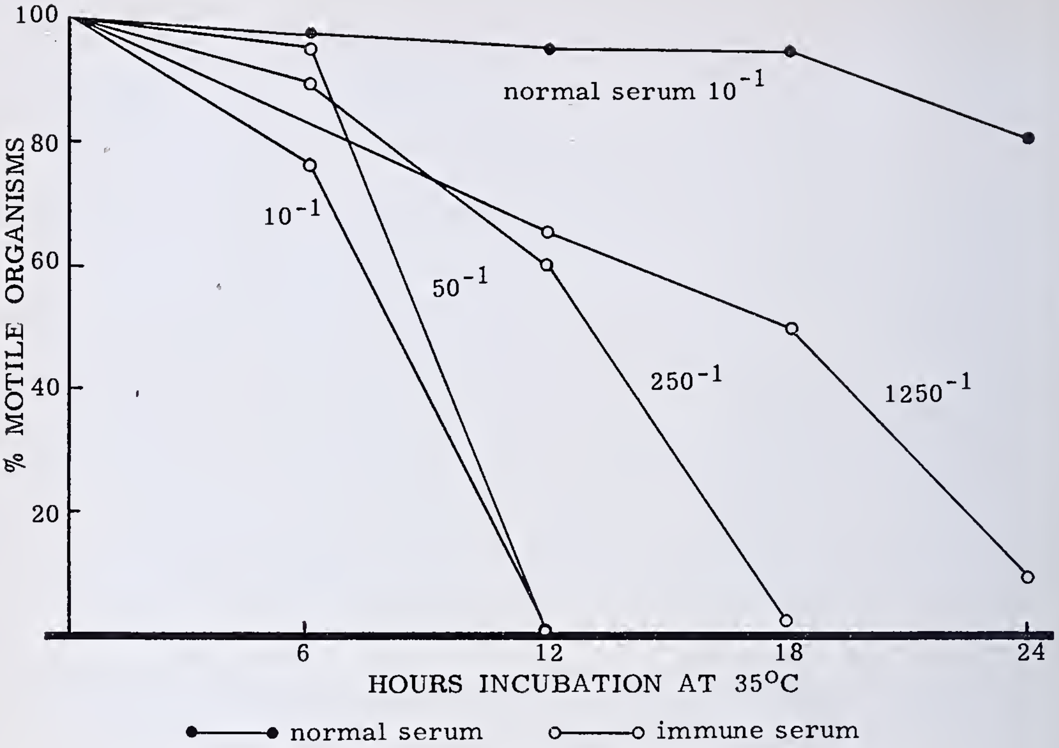

FIGURE 1.—Time required for immobilization of *T. pallidum* by syphilitic serum at 35° C. (Shown are the percentages of motile organisms following exposure to the indicated final concentrations of human syphilitic serums for 6, 12, 18, and 24 hours at 35° C. The results with a 1 : 10 final concentration of normal serum are included as a control.)

interval for the laboratory schedule, it has been selected as the one of choice.

Similar time studies have been made at 37° C., at 30° C., and at 5° C. Immobilization is somewhat accelerated at 37° C. and is markedly retarded at 30° C. and at 5° C.

As was indicated in section B, a more precise technic could be obtained by measuring the dilution of serum required to produce 50-percent killing of the organisms at the end of some arbitrary time period between 12 and 24 hours. As yet we have been unable to do this on any large series of serums.

E. *Nonspecific Results*

As was indicated above, for the purpose of this paper a nonspecific result has been defined as the occurrence of less than 50-percent motility at the end of 18 hours at 35° C. in both the test and control tubes or in the control tube alone. While all serums from patients with early syphilis were obtained from individuals who gave no history of treatment previous to admission, early in our work a considerable number of such serums showed nonspecific killing. It was then determined that the spirochetes in these assays are extraordinarily sensitive to small amounts of penicillin, a final concentration of 0.0015 micrograms of penicillin G per cubic centimeter immobilizing 50 percent of the spirochetes measured at 18 hours at 35° C. This penicillin effect could be completely reversed by the addition of adequate concentrations of penicillinase within the first hour of the start of the assay. When penicillinase was added to these nonspecific serums in a final concentration of 2 units/cc. at the start of the assay, all but one of the nonspecific reactions were corrected. Seventy-seven nonspecific serums were encountered in the syphilitic human serum here reported. Sixty-seven of these have been run with penicillinase at a final concentration of

2 units/cc. Of these 67, 66 reverted either to a definitely positive reaction, to a doubtful reaction, or to a negative reaction. The one serum that remained nonspecific was contaminated with a motile rod in both the test and control tubes. This serum has been excluded from our tabular data.

By stages of the disease, three of the primary syphilitic serums gave a nonspecific immobilization, and, of these, 1 became positive and 2 became negative when run with penicillinase. Twenty-eight serums from patients with secondary syphilis gave nonspecific immobilization. Of these, 24 became positive, 2 doubtful, and 2 negative. Of the patients with early latent syphilis, 22 gave nonspecific immobilization and, of these, 21 became positive and 1 remained nonspecific. The latter was contaminated with the motile rod referred to above and has not been included in the subsequent tabulations. Of the other patients with syphilis (7 with late latent syphilis, 5 with central nervous system syphilis, 2 with congenital syphilis), all became positive when rerun with penicillinase.

Since we are dealing with an enzyme of considerable specificity (*9, 10, 11*), these data would suggest that at least 66 and perhaps more of the 362 syphilitic patients here reported had traces of penicillin in their serums at the time of admission to the hospital. In no instance did the treating clinic have information regarding penicillin. Whether these trace levels are the result of self-medication is unknown. The effect of such penicillin on the course of early syphilis, with particular reference to diagnosis, remains to be determined. It is difficult to account for the fact that, of the 28 patients with secondary syphilis in which there appeared to be traces of penicillin in the blood stream, 18 were darkfield-positive, 6 were darkfield-negative, and, in 4, darkfields were not done. It is difficult to reconcile this observation with the immobilization of *T. pallidum* in vitro unless one assumes that the penicillin levels in the serum were higher than those in the tissues.

F. *Immobilization Tests on 516 Human Serums*

Table 4 shows the results of qualitative tests performed upon the serums from 362 patients with syphilis in various stages, 73 normal patients, and 81 patients with diseases other than syphilis. It is apparent that none of the nonsyphilitic patients gave a positive immobilization test and that, among the syphilitic patients, as the duration of the

Table 4.—***Results of qualitative immobilization tests on serums from 516 humans***

Diagnosis	Result of test						Total patients
	Positive		Negative		Doubtful		
	Number	Percent	Number	Percent	Number	Percent	
Syphilis:							
Primary	10	45.5	11	50	1	4.5	22
Secondary	[1] 156	82.5	26	13.8	7	3.7	189
Early latent	105	99.1	1	0.9	0	0	106
Late latent	20	100	0	0	0	0	20
Central nervous system	18	100	0	0	0	0	18
Cardiovascular	2	100	0	0	0	0	2
Congenital	5	100	0	0	0	0	5
Total syphilis	316	87.6	38	10.3	8	2.1	362
Normal human	0	0	73	100	0	0	73
Human with diseases other than syphilis	0	0	81	100	---	---	81
Total nonsyphilitic	0	0	154	100	0	0	154

[1] Including 2 patients diagnosed as having infectious relapse.

disease increased, there was an increase in proportion of positive results. Ten of the 22 cases of primary syphilis, 156 of 189 cases of secondary syphilis, and 105 of 106 cases of early latent syphilis gave positive immobilization tests. Serums from all patients with later stages of the disease consistently gave a positive result. The numbers of normal patients included are far too few to give a true indication as to the specificity of the test. Our data may be in disagreement with those of Nelson and Mayer (*6*) with respect to secondary syphilis. These authors reported that all of 20 patients with secondary syphilis had a positive immobilization test. A portion of this difference may be ascribed to our more stringent criteria for positivity, but the difference between our findings and those of Nelson and Mayer is not statistically significant, due to the small size of their sample. Our data indicate that, during the early stages of syphilis, the immobilization test is considerably less sensitive as a diagnostic aid than are the conventional serologic tests for syphilis. While the data from the later stages of syphilis appear to be more reliable, the number of patients so far reported is too small to be considered significant.

Table 5 shows the results of the qualitative immobilization tests on serums from patients with syphilis, arranged by the stage of the disease and the titer of the serums in Kahn units. In the primary stage and to some extent in the secondary stage, there is apparent correlation between the titer of the Kahn test and the result of the immobilization test. This apparent correlation is not altogether unexpected, since a similar lag in the production of immobilizing antibodies and reagin might be anticipated. In the later stages of the disease, there is no correlation whatever.

A more adequate criterion of the possible correlation between the titered serologic test and the immobilization test was made by titering the latter in 48 patients representing the various stages of the disease and by comparing the im-

Table 5.—*The relation of the stage of syphilis and reagin titer to the results of the qualitative immobilization test in 353 patients with syphilis*

[The numbers in the body of the table indicate the number of patients falling within the particular grouping.]

Syphilis diagnosis	Result of immobilization tests	Reagin titer in Kahn units												Total number of patients	Median titer
		0	1	2	4	8	16	32	64	128	256	512	1,024		
Primary	−	2	1	----	----	2	1	2	2	----	----	1	------	11	16
	+	----	----	----	----	----	2	2	3	2	1	----	------	10	64
	±	----	----	----	1	----	----	----	----	----	----	----	------	1	4
Secondary	−	1	----	----	1	----	3	4	7	6	----	----	------	22	64
	+	----	----	----	----	----	8	15	[1] 36	50	33	9	3	154	128
	±	----	----	----	----	----	1	----	----	2	1	2	------	6	192
Early latent	−	----	----	----	----	----	----	1	----	----	----	----	------	1	32
	+	2	1	5	2	9	13	23	21	14	7	4	1	102	32
Late latent	+	1	----	----	6	1	4	5	2	1	----	----	------	20	16
Asymptomatic central nervous system.	+	----	----	----	----	----	4	1	4	4	----	----	------	13	64
Symptomatic central nervous system.	+	----	4	----	----	----	----	1	1	----	----	----	------	6	1
Cardiovascular	+	----	----	----	----	----	----	----	1	1	----	----	------	2	96
Congenital	+	----	----	----	----	----	----	----	2	----	1	1	1	5	256
Total	--------	6	6	5	10	12	36	54	79	80	43	17	5	353	64

[1] Including 2 patients diagnosed as having infectious relapse.

Table 6.—*The reproducibility of results with the immobilization test over a 5-month period*

[Included in the table are repeated assays of 3 pools of human syphilitic serums (1, 4, and 11) assayed at fivefold final concentrations from 1/10 to 1/1,250. Each assay was done on a different day over a 5-month period. + equals positive, — equals negative, and D equals doubtful immobilization.]

HUMAN SYPHILITIC POOL 1

Assay number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Serum dilution:																	
1/10	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/50	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/250	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/1,250	D	—	—	—	—	+	+	—	+	—	+	—	D	—	+	—	+

HUMAN SYPHILITIC POOL 4

Assay number	18	19	20	21	22	23
Serum dilution:						
1/10	+	+	+	+	+	+
1/50	+	+	+	+	+	+
1/250	+	+	D	+	+	+
1/1,250	—	—	—	—	—	—

HUMAN SYPHILITIC POOL 11

Assay number	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
Serum dilution:															
1/10	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/50	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/250	+	+	+	+	+	+	+	+	+	D	+	+	+	+	+
1/1,250	—	—	—	+	—	—	+	—	—	—	—	—	—	—	—

mobilization titer against the titer in Kahn units. There was no correlation, as shown by an ungrouped correlation coefficient of 0.097.

G. *Reproducibility of Results*

Table 6 shows repeated quantitative assays on human syphilitic pools 1, 4, and 11, tested over a 5-month period, using different emulsions for each test, different lots of complement, and different personnel setting up the assays. It is seen that, in spite of all the variables entering the test, the titers of the serums are surprisingly reproducible.

H. *The Nature of the Immobilization Substance*

Several lines of evidence indicate that the immobilizing substance in syphilitic serum is an antibody and that it is distinct from reagin. The material is nondialysable, is associated with the serum globulins, requires complement for its demonstration, and is relatively heat-stable. To determine the protein components responsible for activity, alcohol fractionations by method VI of Cohn and others (7) have been made in this laboratory on normal and syphilitic serums. The isolated fractions were dissolved in an amount of M/7 NaCl equal to the volume of the parent serum and titered by the immobilization technic. These data are summarized in table 7. None of the normal serum fractions showed activity, and the activity of syphilitic serums was concentrated principally in fraction II–III, which fraction consists primarily of β and γ globulins. In a few fractionations, traces of active material were found in fraction IV–1, which consists primarily of α globulins and a considerable quantity of lipid material.

Euglobulin fractions of normal and syphilitic serums, by the method of

Erickson (*8*), summarized in table 8, showed only partial removal of the active material in the euglobulin precipitate. Cooperative studies with Dr. Hans Neurath at Duke University are being continued in order to localize the active factors more precisely.

The immobilization antibody is not reagin, as has been shown in absorption experiments. Our results confirm those of Nelson and Mayer (*6*), in that suitable absorption of the reagin with Eagle flocculation antigen (*12*), while removing the antibody responsible for the positive flocculation test, had no effect upon the immobilization tests. Supernatant serums

Table 7.—*Results of the immobilization test on Cohn fractions of normal and syphilitic rabbit and syphilitic human serums*

[The protein fractions of normal and syphilitic rabbit and syphilitic human serums were prepared in this laboratory by method VI of Cohn (7). Each fraction was redissolved in M/7 NaCl and brought to the volume of the original whole serum. The fractions and the original syphilitic human serums were assayed at fivefold final dilutions from 1/10 to 1/1,250. The result of the immobilization test is recorded in such a way that + equals positive, − equals negative, NS equals nonspecific immobilization, and D equals doubtful immobilization.]

Cohn fraction	Final concentration	Normal rabbit	Syphilitic rabbit	Syphilitic human
II and III	1/10	−	+	+
	1/50	−	+	+
	1/250	−	+	+
	1/1,250	−	D	−
IV-1	1/10	−	+	+
	1/50	−	+	−
	1/250	−	−	−
	1/1,250	−	−	−
IV-4	1/10	−	NS	+
	1/50	−	−	NS
	1/250	−	−	−
	1/1,250	−	−	−
V	1/10	−	−	−
	1/50	−	−	−
	1/250	−	−	−
	1/1,250	−	−	−
Whole serum	1/10	−	------------	+
	1/50	−	------------	+
	1/250	−	------------	+
	1/1,250	−	------------	+

Table 8.—*Results of the immobilization test on euglobulin fractions from 2 pools of normal and 2 pools of syphilitic human serums*

[The euglobulin fractions were prepared in this laboratory by the method of Erickson (8). The fractions, the residues, and the original serums from which the fractions were prepared were assayed at fivefold final concentrations, the fractions from 1/5 to 1/625, the residues from 1/100 to 1/12,500, the whole serums from 1/10 to 1/1,250. These concentrations are expressed in terms of their original concentrations in whole serum. The result of the immobilization test is such that + equals positive and − equals negative immobilization.]

	Dilution	Normal human 1	Normal human 2	Syphilitic human 4	Syphilitic human 11
Euglobulin fraction	1/5	−	−	+	+
	1/25	−	−	+	+
	1/125	−	−	+	+
	1/625	−	−	−	+
Residue	1/100	−	−	+	+
	1/500	−	−	+	+
	1/2,500	−	−	−	−
	1/12,500	−	−	−	−
Whole serum	1/10	−	−	+	+
	1/50	−	−	+	+
	1/250	−	−	+	+
	1/1,250	−	−	−	−

from such absorptions were fully as active as the original serums. Normal serums similarly treated showed no immobilization activity. Further, the absorbed reagin, when disassociated from the antibody lipoid complex by strong salt solution in the presence of ether by the method of Davis and others (*13*) showed no immobilizing activity.

Discussion

The finding of circulating antibodies active against *T. pallidum* is not new. The first to demonstrate such an antibody was Eberson (*1*), who in 1921 employed a combined in vivo and in vitro technic to demonstrate the spirocheticidal substance in the serums from persons with late syphilis and from rabbits with syphilis of 6 months' duration or longer. In 1935, Turner (*5*) reported a more sensitive method for demonstrating the presence of this protective substance. This too represented a combined in vitro-in vivo technic in which 9 parts of whole serum were mixed with 1 part of spirochete emulsion, the mixture incubated at 37° C. for 6 hours, and then inoculated intracutaneously into rabbits. While the mixtures containing normal serum and *T. pallidum* produced typical syphilitic lesions at the site of inoculation, the mixtures of immune serum and spirochetes produced smaller lesions with prolonged incubation periods or produced no lesions whatsoever. Since positive tests were found in 10 of 11 known-syphilitic persons who had negative serologic tests for syphilis, the protective antibodies demonstrated by Turner (*14*) appeared to be distinct from reagin. Turner's technic also indicated the probable role played by complement, since inactivation of the serum prior to testing gave significantly less protection.

The work of Nelson and Mayer (*6*) has made available an in vitro method for the demonstration of immobilizing antibodies for virulent *T. pallidum*. The available evidence would suggest that the so-called immobilizing antibody is similar to if not identical with the antibodies found in the combined in vitro-in vivo technics. The fact that these antibodies develop during the course of both experimental and human syphilis and have a deleterious effect upon the treponeme in vitro suggests that they may play a role in acquired immunity to syphilis. It does not follow, however, that the titer of the immobilization test is a direct measure of the patient's or of an animal's immunity. Preliminary work in this laboratory, to be reported separately, has indicated that there may be a wide disparity between the two.

Other facts that suggest the need for caution in accepting the immobilization test as a measure of immunity are these: in patients with late symptomatic syphilis, in whom the immune process presumably failed to arrest progress of the disease, the immobilization test was regularly positive; in patients with secondary syphilis, the incidence of positive immobilization tests was as high in patients with darkfield-positive lesions as in patients with darkfield-negative lesions.

It is to be hoped that the immobilization technic may be of assistance in the differentiation of biologic false-positive serologic tests for syphilis. While studies in this direction are being conducted in this laboratory, our data are too limited at this time to be of value.

The present cumbersome nature of the immobilizing technic precludes its use in all except a few research laboratories. The chief difficulties arise from the fact that animals must be used as a source of the virulent *T. pallidum*. In the hands of research laboratories, the technic may yield much valuable information with respect to the mechanisms of immunity in syphilis and in the evaluation of biologic false-positive serologic tests for syphilis.

Summary

1. The in vitro test for immobilizing antibodies against *T. pallidum* reported by Nelson and Mayer (*6*) has been run on 362 patients with syphilis, 81 patients with diseases other than syphilis, 73 normal humans, and 91 normal rabbits. No positive tests have been encountered in any of the nonsyphilitic individuals. In

syphilitic patients, the immobilizing antibody develops fairly early in the course of the disease, and the percentage of positive immobilization tests increases with the duration of the disease.

2. Modifications in technic have been suggested that would permit more extended assays with the same amount of materials. The variability of the tests in normal humans and animals has suggested upper limits of normality.

3. The immobilizing substance appears to be an antibody, is associated with the globulin fractions of serum protein, and is concentrated to the greatest extent in fraction II–III of Cohn, to a lesser extent in IV-1. It is only partially removed in the euglobulin fraction.

4. While the immobilization technic may offer an important tool for the research laboratory in the investigation of problems of immunity in syphilis and in the study of biologic false-positive serologic tests for syphilis, the reliability and significance of the test need further evaluation.

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Penicillin in the Treatment of Early Syphilis: 639 Patients Treated with 2,400,000 Units of Sodium Penicillin in 7½ Days[1]

Herman N. Bundesen, M. D.,[2] Frederick Plotke, M. D.,[3] George X. Schwemlein, M. D.,[4] and Jack Rodriquez, M. D.[5]

As one of a series of investigations concerning the use of penicillin in early syphilis there are herewith presented preliminary data on the use of total dosages of 2,400,000 units of sodium penicillin administered in aqueous solution—40,000 units intramuscularly every 3 hours over a period of 7½ days for 60 injections.

It had been previously ascertained that amounts of aqueous penicillin smaller than 2,400,000 units over a 7½-day period were inadequate in the treatment of early syphilis (*1, 2, 3, 4, 5*). In the present investigation, 639 patients with darkfield-positive early syphilis were treated by the described schedule of treatment from November 15, 1944, through March 23, 1946. No further treatment was administered unless either clinical or serologic relapse occurred or pregnancy intervened. The results of observation of these patients over a maximum period of 27 months and a minimum period of 24 months are presented.

The distribution of these patients by race, sex, and age is indicated in table 1. The age of the patients ranged from 15 to 60 years: 13.2 percent were under 20 years; 35.2 percent were from 20 to 24 years; and 51.6 percent were 25 years and over.

Table 1.—***Early syphilis patients treated with 2,400,000 units of sodium penicillin in 7½ days***

Race and sex	Age in years			
	Total	Under 20	20–24	Over 24
Total	639	84	225	330
Male	419	33	110	276
Female	220	51	115	54
White	121	3	29	89
Male	93	1	19	73
Female	28	2	10	16
Other	518	81	196	241
Male	326	32	91	203
Female	192	49	105	38

There were 92 (14.4 percent) cases of primary seronegative syphilis (including 6 reinfections); 179 (28.0 percent) cases of primary seropositive syphilis (including 14 reinfections); 266 (41.6 percent) cases of secondary syphilis (including 27 reinfections); and 102 (16.0 percent) cases of relapsing early syphilis. The relapsing patients included 6 monorecidives, 32 patients who progressed from primary to secondary syphilis, and 64 cases of relapsing secondary syphilis.

Four hundred and eighty-four patients had received no previous treatment; 155 had received some type of antisyphilitic treatment prior to their present hospital admission but had subsequently been reinfected or had evidenced relapse or inadequate resolution of their initial lesions. The previous treatment had consisted of arsenicals, penicillin, bismuth, and fever therapy alone or in various combinations over short and long periods.

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[1] From the Chicago Intensive Treatment Center, Venereal Disease Control Program, Chicago Board of Health, in cooperation with the U. S. Public Health Service.

[2] President, Chicago Board of Health; Senior Surgeon (R) (Inactive), U. S. Public Health Service.

[3] Venereal Disease Control Officer, Chicago.

[4] Research Associate, Kettering Foundation for Medical Research, Cincinnati; Instructor, Department of Internal Medicine, College of Medicine, University of Cincinnati.

[5] Instructor in Dermatology, University of Illinois; Medical Director, Chicago Intensive Treatment Center; Research Associate, Kettering Foundation for Medical Research, Chicago.

Table 2.—***Early syphilis patients treated with 2,400,000 units of sodium penicillin in 7½ days, grouped by number of days of observation and treatment results***

Number of days from beginning date of therapy	Number of patients			
	Total observed during period or later	Serologic titer		Failures found during period
		Negative	Positive	
0–29	639	102	536	1
30–59	587	173	406	8
60–89	559	228	324	7
90–119	530	264	251	15
120–149	504	283	207	14
150–179	480	308	167	5
180–209	469	321	139	9
210–239	447	323	119	5
240–269	431	316	108	7
270–299	408	306	98	4
300–329	397	298	91	8
330–359	378	291	83	4
360–449	369	294	61	14
450–539	342	287	49	6
540–629	289	252	28	9
630–719	202	183	10	9
720–809	116	105	7	4

The results of treatment are summarized and demonstrated graphically in table 2 and figures 1 and 2.[6] The cumulative failure rate at the end of 2 years was 23.2 percent among 92 patients with primary seronegative syphilis; 26.9 percent among 179 patients with primary seropositive syphilis; 37.5 percent among 266 patients with untreated secondary syphilis; and 33.6 percent among 102 patients who had had previous treatment and subsequently relapsed. The over-all failure rate, regardless of diagnosis, was 32.2 percent at the end of the 27 months' observation period.

Of 547 patients with positive pretreatment serologic titers, 374 (68.4 percent) reversed to negative. The median number of days required to reach seronegativity was 103[7] for the group; 60 for 141 patients with primary syphilis; 130 for 175 patients with secondary syphilis; and 170.5 for 58 patients[8] with relapsing syphilis. One hundred and sixty-one patients (43.0 percent) reached seronegativity within 3 months and 281 (75.1 percent), within 6 months. Fifty-five patients (14.7 percent) were later treatment failures, including 20 clinical relapses, 16 serologic relapses, 18 reinfections, and 1 patient with cerebrovascular syphilis.

Cerebrospinal fluid examinations were made for all except 31 of the 639 patients—before treatment for 390 patients and during treatment for 218 patients. Sixty-five (10.7 percent) of the 608 patients examined showed abnormal findings. Six had positive Kahn tests, 27 had a cell count above 7 lymphocytes, and 41 had more than 45 mg. percent protein. Twenty-eight of the 65 patients have since been reexamined, with 19 registering normal findings and 9, abnormal findings. Of the 543 patients with normal pretreatment spinal fluids, 229 were later examined; 17 (7.4 percent) had developed abnormalities.

Of the 639 patients treated, 129 were known treatment failures. These included 12 patients with relapsing primary syphilis, 16 with primary syphilis progressing to secondary syphilis, 35 with relapsing secondary syphilis, and 40 serologic failures. Two neurorecurrences and 24 probable reinfections are included. It is recognized, however, that more of the treatment failures may well have been reinfected.

There were no serious complications resulting from the treatment administered. Treatment was discontinued because of lack of cooperation in 4 cases and because of penicillin sensitivity in 1

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[6] The percentages used for the figure showing success and failure were obtained by assuming that patients lost from observation would have shown the same ratio of treatment results as those observed. The percentage observation of each period to the preceding period has been applied to the cumulative failure figure, so that the same proportion of failures has been carried forward as total patients observed. Patients with positive significant serologic titers (4 Kahn units or more) after 12 to 15 months have been grouped with failures. Those who were seronegative or maintained nonsignificant titers (3 Kahn units or less) were for the present considered successes.

[7] Data biased because of irregularity of follow-up.

[8] Exclusive of two patients who became negative after 27 months.

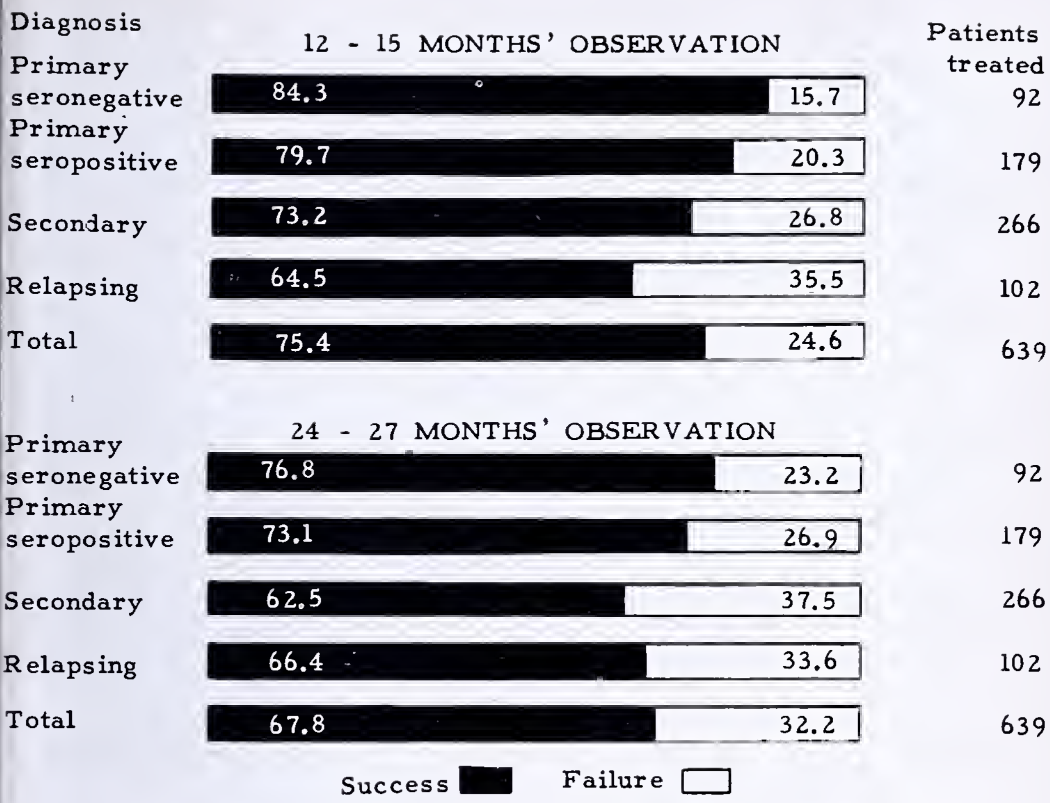

FIGURE 1.—Early syphilis patients treated with penicillin. Cumulative percentages of successes and failures, 12 to 15 months' and 24 to 27 months' observation. (By diagnoses.)

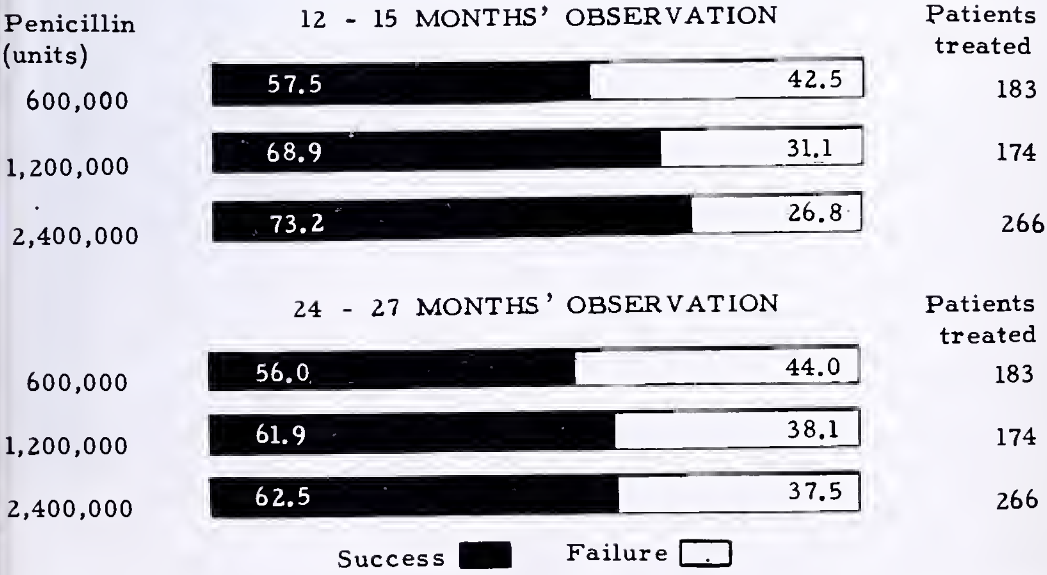

FIGURE 2.—Early syphilis patients treated with penicillin. Cumulative percentages of successes and failures, 12 to 15 months' and 24 to 27 months' observation. (By treatment schedules.)

case. The 639 patients completed treatment on schedule within 7½ days. Five patients developed Herxheimer reactions, with fever and cutaneous manifestations. Eighty-seven patients registered temperatures from 1° to 2° above the pretreatment average sometime during the first 48 hours; 110 registered temperatures of 2° or more. Twenty-five patients showed secondary fever and 3, pruritus.

Comment

Three methods of treatment employed at this center for darkfield-positive early syphilis are worthy of comparison.[9] In a group of 330 patients given 600,000 units of sodium penicillin in 7½ days, the over-all failure rate was 39.8 percent at the end of 2 years. In a group of 323 patients receiving 1,200,000 units of sodium penicillin by the same method, the failure rate was 31.1 percent. In the group presented in this paper (639 patients), the failure rate was 32.2 percent at the end of 2 years.

Analyzing the results in untreated secondary syphilis on these same 3 schedules, the failure rate was 44.0 percent among 183 patients receiving 600,000 units of penicillin; 38.1 percent among 174 patients receiving 1,200,000 units of penicillin; and 37.5 percent among 266 patients receiving 2,400,000 units of penicillin.

Attempts at shortening the method by giving 1,200,000 units over 3¾ days were encouraging in that at the end of 2 years there was an over-all failure rate of 29.8 percent among 412 patients and 30.8 percent among 210 patients with secondary syphilis. Further attempts at compressing the treatment to 24 hours and increasing the dose of penicillin to 10, 15, 20, and 25 million units were completely unsuccessful (*6, 7*).

It is obvious that diligent investigation regarding the parasite life cycle, host-parasite, and parasite-tissue penicillin concentration relationship is necessary if perfection is to be approached in the rapid treatment of syphilis with the use of penicillin.

Summary

1. Six hundred and thirty-nine patients with darkfield-positive primary and secondary syphilis were each given 2,400,000 units of sodium penicillin over a period of 7½ days.

2. The over-all failure rate, regardless of diagnosis at the 2-year observation period, was 32.2 percent.

3. The form of treatment described is considered inadequate.

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4. Craig, R. M.; Schwemlein, G. X.; Barton, R. L.; Bauer, T. J.; Bundesen, H. N.: Penicillin in the treatment of early syphilis, 429 patients treated with 1,200,000 units in 90 hours. Ann. Int. Med., 27: 225–230, August 1947.

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[9] The results presented in this paper must be interpreted in light of the fact that from June 1943 to the present time, commercial penicillin has been a changing mixture of various substances. The content of "impurities" has gradually decreased as potency, in terms of units per milligrams, has increased. The relative amounts of the several identified penicillin fractions, G, F, X, and K, have likewise varied from time to time. Those two changes, and perhaps others, suggest that therapeutic efficacy may not have remained constant and that it may be significantly different today than it was originally. It is not now possible to assess the extent to which these changes may have affected the results here reported.

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The Effect of Temperature Variants on Quantitative Turbidimetric Determinations of Spinal Fluid Protein, Using Trichloracetic Acid[1]

Virginia L. Harding, Serologist, and Ad Harris, Senior Serologist, United States Public Health Service

The use of trichloracetic acid as a precipitant for the turbidimetric determination of protein content of spinal fluid has been reported (*1*). The advantage of this method over the procedures using sulfosalicylic acid lies in the fact that it is not influenced by alteration of albumin-globulin ratio. Observations made during the use of the trichloracetic acid method indicated that variations in the temperature at which the test was conducted might influence calculated end results.

The purpose of this article is to report findings obtained during an investigation of the effects of temperature on quantitative turbidimetric analysis of protein, using trichloracetic acid, and to record the method now used in the Venereal Disease Research Laboratory for the routine determination of total protein content of spinal fluids.

Reagents

1. 10-percent trichloracetic acid solution in distilled water.
2. 0.9-percent sodium chloride solution in distilled water.
3. Human serum of known protein content (micro-kjeldahl analysis).

Procedure

Protein solutions containing 10, 20, 30, 40, 50, and 60 mg. per 100 ml. were prepared by adding appropriate amounts of 0.9-percent sodium chloride solution to Seitz-filtered human serum containing 7.32 gm. of protein per 100 ml. Tests were then performed simultaneously, at 37° C., 27° C., 21° C., and 16° C. The method employed in this testing is described under "Procedure for the Routine Determination of Spinal Fluid Protein."

Light transmission values obtained on tests performed at 37° C., 27° C., 21° C., and 16° C. are recorded in table 1. These findings indicate that greater turbidity was produced and that lower light transmission values were consequently obtained at the higher temperatures.

The effects that these temperature changes might have on estimated protein content may be visualized from the figures listed in table 2. Results presented in this table were obtained by projecting

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[1] From the Venereal Disease Research Laboratory, U. S. Marine Hospital, Staten Island 4, N. Y. Senior Surgeon R. C. Arnold in charge.

Table 1.—***Photoelectric colorimeter readings obtained with solutions of known protein content treated with 10-percent trichloracetic acid at several temperatures***

Serum dilutions containing known amounts of protein [1] (mg. percent)	Temperature at which testing was performed			
	37° C.	27° C.	21° C.	16° C.
10	[2] 85	86	88	89
20	71	75	78	79
30	60	64	69	71
40	52	56	59	63
50	43	49	53	57
60	37	43	47	50

[1] Obtained by micro-kjeldahl analysis.

[2] Figures indicate percent light transmission. All readings recorded represent the average of triplicate analyses.

Table 2.—***Calculated total protein values from tests performed at several temperatures, using conversion chart prepared from findings obtained by testing at 21° C.***

Serum dilutions containing known amounts of protein [1] (mg. percent)	Temperature at which testing was performed			
	37° C.	27° C.	21° C.	16° C.
10	[2] 12. 5	12	10	9
20	27	22. 5	20	18. 5
30	40	35	29	27
40	51. 5	46	41. 5	36. 5
50	66. 5	56	50	44. 5
60	78. 5	66. 5	60	55

[1] Obtained by micro-kjeldahl analysis.

[2] Figures indicate milligrams of protein per 100 ml. (mg. percent). All figures recorded represent the average of triplicate analyses.

light transmission values produced by testing at the four listed temperatures on a graph prepared from findings obtained at 21° C.

Since the elimination of the variable introduced by temperature change was desired and since the lower temperatures could not be readily maintained during all months of the year in the testing laboratory, the highest temperature used was selected for routine testing. The step-by-step procedure employed in the Venereal Disease Research Laboratory for the routine determination of spinal fluid protein is as follows:

Procedure for the Routine Determination of Spinal Fluid Protein

1. Pipette 2.5 ml. of spinal fluid into a 13 x 100 mm. test tube.

Note: Contaminated (visibly turbid) spinal fluid is unsatisfactory for testing.

2. Add 2.5 ml. of 10-percent trichloracetic acid solution.

3. Gently invert tube twice to mix contents (avoid foaming).

4. Allow to stand 10 minutes in 37° C. water bath. Again gently invert tube.

5. Pour fluid into photoelectric colorimeter cuvette and determine percent transmission at approximately 420-mu. wave length.

Note: (*a.*) The usual zero reading adjustments are made before transmission readings of spinal fluid samples are taken.

(*b.*) Any photoelectric colorimeter having cuvettes that will accommodate a 5-ml. volume may be used. Lesser amounts of spinal fluid may be tested if the same proportion of fluid to acid solution is retained, provided that the photometer employed is adaptable to the use of smaller cuvettes.

6. Convert percent transmission to milligrams percent (mg. percent) total protein by reference to a calibration chart.

Note: This chart may be prepared by testing several concentrations of a serum of known protein content (from 10 to 50 mg. per 100 ml.) exactly as described above and by plotting the percent transmission values of the turbidities thus obtained on semilogarithmic paper.

7. Serum aliquots of known protein content (micro-kjeldahl) diluted to 10, 30, and 50 mg. protein per 100 ml. are included as daily controls to check the performance of the photoelectric colorimeter and reagents.

8. Spinal fluids having more than 50 mg. protein per 100 ml. are diluted and retested, since reproducibility of results is best in the range of 0 to 50 mg. per 100-ml. concentration.

Discussion

Although temperature was found to influence the turbidity formed upon the addition of trichloracetic acid to spinal fluid, accurate quantitative results may be obtained at uncontrolled room temperatures provided the standard protein solutions are tested, simultaneously, each day. Under these circumstances, protein values for the spinal fluids tested must be calculated by comparison with findings obtained on solutions of known protein content that are retested on each testing day. Since this method requires replotting calibration curves each day it is more practical, for routine testing, to prepare the conversion chart from points obtained by tests performed at 37° C. and to conduct daily testing at this temperature.

The recommendation that the conversion chart be limited to the maximal value of 50 mg. percent protein and that spinal fluids containing larger amounts of protein be diluted and retested was made since greater reproducibility of results may be expected in this zone. Variations of 1 percent in light transmission values, in the range below 40 percent, convert into differences as great as 3 to 4 mg. percent protein. In the light transmission range above 40 percent, this error is reduced. Since many of the colorimeters used in routine testing cannot be operated with accuracies greater than ±1 percent light transmission, the use of only the higher light transmission range will reduce errors of conversion to acceptable limits.

Summary

1. The effects of temperature variants on the quantitative turbidimetric determination of protein, using trichloracetic acid as a precipitant, are demonstrated.

2. The technic for the routine determination of spinal fluid protein, as employed in the Venereal Disease Research Laboratory, is presented.

Reference

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CURRENT NOTES AND REPORTS

Social Hygiene Day 1950

More than ever, with the broad-scale attack on syphilis through case-finding campaigns across the Nation, the local community observances of Social Hygiene Day, February 1, 1950, assume vital importance.

These observances are designed to enlist citizen support of social hygiene objectives which this year stress education to prevent venereal infections, particularly through training of youth through home, church, and school for successful marriage and family life. The slogan for Social Hygiene Day 1950 is "Social Hygiene is a Family Affair."

Held under the national sponsorship of the American Social Hygiene Association, with the cooperation of the United States Public Health Service, the observances in thousands of cities and towns in the United States and the Territories serve to focus public attention on the need for social hygiene programs and to spark year-round efforts.

The largest of the meetings, held in conjunction with the annual meeting of the Association, will be in New York City at the Hotel New Yorker on Wednesday, February 1.

All avenues of reaching the public, including newspapers, magazines, radio, and, wherever possible, television, will serve to channel out publicity on the events of the Day, which in many areas will be officially proclaimed by governors of States and mayors of cities. To aid in planning these local events, the Association is preparing an attractive illustrated publication for wide distribution, along with informational materials.

Prominent speakers will be enlisted for the local celebrations which will be highlighted by stimulating discussions, forums, and similar technics to bring about greater understanding of social hygiene problems among citizens.

The local meetings are conducted under the aegis of leaders from all phases of community life, following the pattern of the Association and the State and local social hygiene societies which work in close cooperation with the medical profession, public health officials, voluntary welfare groups, pharmacists, the clergy, and leaders in industry, labor, education, civic affairs, and law enforcement, as well as parent-teacher and youth-building organizations.

Any communities which have not yet instituted annual observance but which wish to participate in or to launch a social hygiene society, may get suggestions and free materials by writing to the Social Hygiene Day Service, American Social Hygiene Association, 1790 Broadway, New York 19, N. Y.

New Serologic Tests Manual Available

Supplement 22 to The Journal of Venereal Disease Information, "Manual of Serologic Tests for Syphilis,' 'is now being distributed. Attractively bound in plastic, the manual has index-tabbed chapters on serologic tests for syphilis being performed in the United States. During the 4 years that have elapsed since the laboratory manual "Technics of Serodiagnostic Tests for Syphilis—1944" was published, many changes in testing methods have been introduced. Principal among these have been the changes associated with the use of antigens prepared from cardiolipin and lecithin.

The manual, prepared with the assistance of the originators of each test technic, was assembled at the Venereal Disease Research Laboratory, U. S. Marine Hospital, Staten Island 4, New York. This new manual supersedes Supplements 9 and 11 to Venereal Disease Information published in 1939 and 1940 and VDgraphic-85, published in 1944.

Supplement 22 is well suited for use under laboratory conditions and should be a welcome addition to every technician's library.

Copies of the manual may be obtained from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. The price per single copy is $1.50.

Football Edition of "Facts . . ."

A football edition of the popular "Facts on American Sports and Health" has just been published by the Health Publications Institute in Raleigh, N. C. Printed in color, this eight-page booklet carries schedules on the major colleges and both professional conferences. Notes on teams and players are interspersed with health pointers. Drawings and cartoons help make this a lively, readable publication for use in health education work, especially among teen-age and adult sports fans. These new 8″ x 11″ program-style booklets can be obtained from the Health Publications Institute, 216 N. Dawson St., Raleigh, N. C., for $50 per 1,000 copies.

New Premarital-Prenatal Laws for Texas

Texas legislators have passed bills requiring premarital and prenatal examinations for syphilis. With these acts, 37 States and the Territory of Hawaii have laws calling for premarital blood tests of both bride and groom. Thirty-nine States, Hawaii, and the Virgin Islands protect babies from syphilis by laws providing for blood tests of expectant mothers.

Texas House Bill 588, approved on July 8, 1949, to be effective October 5, 1949, is the first law in that State enforcing blood tests for both parties of a marriage. Previous requirements had demanded a test only of the bridegroom.

The prenatal blood test law, House Bill 597, is also a "first" for the State and was effective on the same date. The physician or midwife must state on the birth certificate whether a blood test for syphilis was made during the mother's pregnancy.

Violations under either act are considered misdemeanors, punishable by $200 to $500 fines.

Revision of Illinois Marriage Law

According to a recent memorandum from Dr. Roland R. Cross, Director of the Illinois State Department of Public Health, the Illinois Act in Relation to Marriages was amended on July 23, 1949, to delete the requirement of a microscopic test for gonococci.

CURRENT LITERATURE

Note: Abstracts of all articles listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

Acta path. et microbiol. Scandinav., Copenhagen

Non-specific serologic reactions in syphilis. Olof Sievers. 25 : 795–800, Fasc. 6, 1948.

Serological studies on gonococci. I. Technique. Gono-reactions of 'normal' rabbits. Serological relation between gonococci and *Pasteurellae*. Alice Reyn. 26 : 51–70, Fasc. 1, 1949.

Serological studies on gonococci. II. Cross absorption experiments and factor serum determinations. Alice Reyn. 26 : 234–251, Fasc. 2, 1949.

Serological studies on gonococci. III. Thermostability and bio-chemical nature of the gonococcus antigens. Durability of the factor sera. Discussion. Alice Reyn. 26 : 252–268, Fasc. 2, 1949.

Sensitivity of *Hemophilus ducreyi* to penicillin, streptomycin, and sulfathiazole. Flemming Reymann. 26 : 309–318, Fasc. 2, 1949.

An investigation of the biochemical reactions of *Hemophilus ducreyi*. Flemming Reymann. 26 : 345–353, Fasc. 2, 1949.

Am. J. Pub. Health, New York

Interstate reciprocity for approved laboratories. William Levin. 39 : 635–642, May 1949.

Am. J. Syph., Gonor. & Ven. Dis., St. Louis

- *The rate of multiplication of *Treponema pallidum* in normal and immune rabbits. Mary C. Cumberland and Thomas B. Turner. 33 : 201–212, May 1949.
- *Morphologic changes in syphilitic lesions during the Jarisch-Herxheimer reaction. Walter H. Sheldon and Albert Heyman. 33 : 213–224, May 1949.
- *The Jarisch-Herxheimer reaction in early congenital syphilis. A study of ninety-three patients treated with penicillin alone. Osvaldo A. Pardo and Harold A. Tucker. 33 : 225–233, May 1949.
- *Penicillin treatment of syphilitic primary optic atrophy. An interim report. Joseph V. Klauder and Benjamin A. Gross. 33 : 234–242, May 1949.
- *Ratio of gonorrhea to syphilis as occurring in the United States Navy. Robert W. Babione. 33 : 243–262, May 1949.
- *Aureomycin treatment of acute gonorrhea in males. Harvey Shields Collins, Helen Trousdale, Thomas F. Kaiser, Francis C. Regan and Maxwell Finland. 33 : 263–269, May 1949.
- Benign late gummatous syphilis occurring more than 40 years after infection. Richter H. Wiggall and Richard D. Hahn. 33 : 270–273, May 1949.
- Agranulocytic angina, a rare complication of therapeutic malaria : case report. Israel Kopp. 33 : 274–279, May 1949.
- The possibility of blood bank transmission of lymphogranuloma venereum infection. Louis T. Wright. 33 : 280–281, May 1949.

The rate of multiplication of *Treponema pallidum* in normal and immune rabbits. Mary C. Cumberland and Thomas B. Turner. Am. J. Syph., Gonor. & Ven. Dis., 33 : 201–212, May 1949.

This study was made to determine what happens to spirochetes during the first few days following introduction into susceptible and resistant hosts. For experiments on normal rabbits, testes were removed at the height of the syphilitic orchitis following inoculation with the Nichols strain of *Treponema pallidum*. By comparing the number of spirochetes inoculated with the number counted when the testis was removed immediately after inoculation, the proportion of organisms was shown to bear a direct relationship to the number introduced. At various intervals after inoculation the testes were removed and cut into six equal transverse sections. A loopful of 10-percent serum-saline was pressed into the surface of each section and between 0.0025 and 0.005 ml. of the tissue-rich fluid collected on a coverslip. The total number of spirochetes counted in a given number of fields of all six preparations from a single testis was taken as an index of the spirochete population of the whole testis.

In one group the testes were removed immediately after inoculation and spirochete counts made at once. In another group the testes were ligated at both ends immediately after inoculation and removed. In a third group the testes were inoculated, left undisturbed in situ for 2, 4, or 6 hours, and then removed for counting.

It was apparent that spirochetes are not destroyed in the testis itself and do not disappear when the efferent vascular and lymphatic vessels are ligated. Following the rapid initial drop, the spirochetes become increasingly numerous with the passage of time.

In order to obtain immune animals in which the testes had not been the site of a previous syphilitic lesion, rabbits were inoculated intracutaneously on the back with the Nichols strain. All rabbits were treated with a curative dose of penicillin 68 to 80 days after injection (2 animals treated 115 days after injection). At the time of introduction of the graded number of spirochetes into the testis, about 5,000 treponemes were inoculated intracutaneously into the back of the same animal in order to show that it possessed at least some degree of immunity. In general, the animals did not show complete chancre immunity, although all gave evidence of partial immunity.

Results showed that there was no significant difference in the number of spirochetes found in normal and immune testes which had been excised and maintained outside the animal body for 2 to 4 hours before sectioning and making counts. It is likely that the rapid loss of spirochetes observed in intact immune testes was due to the same factors as were operating to cause loss in the normal testis and was not due to action of factors associated with tissue or humoral immunity.

About 93 percent of the treponemes inoculated into either normal or immune rabbit testes disappeared within 2 hours. Counts made on normal and immune testes at 1 day after inoculation showed no significant difference, but by 3 days postinoculation the number of spirochetes found in immune testes was definitely lower than was the number found in normal testes. The 7- and 11-day counts showed very striking differences in that the spirochetes in the normal testes became exceedingly numerous, whereas in the majority of the immune testes none or only a few organisms were found.

On various days following introduction of 10 million *T. pallidum* into each testis of supposedly immune rabbits, one testis was removed. The remaining testis was removed several days later so that it was possible to infer whether there had been an increase or decrease in the spirochete count of that particular animal.

The rate of multiplication of *T. pallidum* in the normal rabbit testis was found to be approximately 33 hours per single division.

Morphologic changes in syphilitic lesions during the Jarisch-Herxheimer reaction. Walter H. Sheldon and Albert Heyman. Am. J. Syph., Gonor. & Ven. Dis., 33: 213–224, May 1949.

The morphologic changes occurring during the Herxheimer reaction were studied in 31 patients, 29 of whom had untreated primary and secondary syphilis, while the remaining 2 patients had late nodular syphilides. Thirty patients were Negroes, 1 was white, 17 were female, and 14 were male. The specimens taken for histologic study were: 1 primary lesion, 28 secondary lesions, and 2 late nodular syphilides. The diagnosis of syphilis was established by positive darkfield examinations in 25 of the patients, and by the history, clinical manifestations, and a positive serologic test in the 6 remaining patients.

Penicillin in aqueous solution in doses of 80,000 units every 3 hours was given to 21 patients. A single injection of 60 mg. of mapharsen was given to 9 patients, while the remaining patient received 2 cc. of sodium bismuth tartrate.

Before treatment, the clinical symptoms, oral temperature, and the gross appearance of the lesions were carefully recorded, and a biopsy of the syphilitic lesions was taken. Biopsies of the syphilitic lesions were repeated at various intervals during the next 12 to 24 hours.

The pattern of the histologic changes following treatment was the same in all types of syphilitic lesions. The study of lesions at various intervals during the Herxheimer reaction revealed a definite sequence in the morphologic alterations. At first the capillaries and small blood vessels showed marked congestion; later they were crowded with neutrophilic polymorphonuclear leucocytes. The changes which were sharply confined to the syphilitic lesions appeared within 4 hours after treatment and subsided within 18 hours.

The criteria for the occurrence of a clinical Herxheimer reaction consisted of elevation of oral temperature to 100° F. or more, even if no other clinical evidence of the reaction occurred. Exacerbation of lesions or systemic manifestations occurred in 12 patients with an elevation of temperature. A definite clinical Herxheimer reaction was observed in 21 patients, all but 1 of whom showed histologic changes. This patient had recurrent annular secondary lesions and was treated with mapharsen. Neither clinical nor histologic evidence of the phenomenon was observed in 3 patients. The occurrence of a clinical reaction was regarded as questionable in 7 patients in whom the temperature elevation was less than 100° F.

A definite Herxheimer reaction was encountered in more than 70 percent of the patients in this series, but the incidence was lower in a similar group of patients who are part of another study. The present experience indicated that careful observation of patients undergoing initial treatment for early syphilis will reveal a Herxheimer reaction in more than 50 percent of the cases.

A close correlation of the clinical and morphologic aspects of the Herxheimer reaction was revealed.

The Jarisch-Herxheimer reaction in early congenital syphilis. A study of ninety-three patients treated with penicillin alone. Osvaldo A. Pardo and Harold A. Tucker. Am. J. Syph., Gonor. & Ven. Dis., 33: 225–233, May 1949.

Between September 1943 and March 1948, 129 children under 3 years of age were diagnosed as having early congenital syphilis and given antisyphilitic therapy at the Johns Hopkins Hospital. Of these, 36 were excluded from this study for various reasons. The diagnosis of congenital syphilis in the 93 patients retained in the study was established in all cases on the basis of laboratory data. Darkfield examinations in 12 children with mucocutaneous lesions were positive for *Treponema pallidum*. A total of 37 had clinical lesions proved to be or compatible with the diagnosis of early congenital syphilis. All were seropositive in consistently high or rising titer, and in 12, the Wassermann reaction of the cerebrospinal fluid was positive. None of these patients had been given previous syphilis therapy. A fever of 38° C. (100.4° F.) or greater, occurring from 4 to 36 hours after the start of penicillin treatment in a patient previously afebrile and lasting less than 36 hours, was regarded as a Jarisch-Herxheimer reaction.

All records were examined with particular reference to the time when lumbar punctures were performed in relation to the institution of treatment. Of the 15 patients who developed fever of 38° C. or greater, no correlation could be seen between lumbar puncture and the onset or height of fever.

Nine of the original 129 patients died during or after the completion of penicillin therapy, but in each case, prematurity, malnutrition, general debility, or intercurrent disease were complicating factors. None of the deaths were believed to be directly attributable to the Jarisch-Herxheimer reaction.

No relationship was observed between incidence and magnitude of the reaction and age, race, sex, type of congenital syphilis, serologic titer, or outcome. All patients were treated with amorphous or crystalline penicillin G in aqueous solution. No correlation was demonstrable between incidence and magnitude of reaction and the gravimetric dosages of penicillin administered. The time of onset or height of fever in reactors was not influenced by the size, the interval between, or the number of doses.

Long-term follow-up data were available in 69 of the 93 records selected for study. During a mean posttreatment observation period of 524 days, 39 of the patients became and remained seronegative. In 8 of the patients, follow-up studies indicated re-treatment, since 4 were seroresistant and 4 relapsed serologically. Re-treatment with twice the original amount of penicillin was ordinarily used. Data suggested that the occurrence of febrile Jarisch-Herxheimer reactions had little or no bearing on the serologic outcome.

Penicillin treatment of syphilitic primary optic atrophy. An interim report. Joseph V. Klauder and Benjamin A. Gross. Am. J. Syph., Gonor. & Ven. Dis., 33: 234–242, May 1949.

From April 1944 to November 1948, 56 patients with syphilitic primary optic atrophy were treated with penicillin. Of this number, 53 had acquired syphilis, while 3 had congenital syphilis. The forms of neurosyphilis in the acquired syphilis group were: tabes dorsalis, 34 patients; meningovascular neurosyphilis, 18 patients; paresis, 1 patient. Of the 3 patients with congenital syphilis, 1 each had tabes dorsalis, meningovascular neurosyphilis, and taboparesis.

At the beginning of the study in April 1944, the partially purified sodium salt of penicillin in aqueous solution was used, and injections were given every 3 hours for 7½ days for a total dose of

4,200,000 units. No other treatment was given unless the optic atrophy progressed unfavorably. Re-treatment with penicillin, as well as fever and metal chemotherapy, was given. Of the 56 patients, 34 were treated according to this schedule.

A second schedule of treatment was started about August 1946 and consisted of 3.6 gm. of crystalline penicillin G (the equivalent of about 6 million units of sodium penicillin). Injections were given every 3 hours for 7½ days. If the physical condition warranted, fever therapy was given conjointly with penicillin. Twenty-two patients were treated with this schedule.

Evaluation of whether or not the disease was progressive was determined essentially from the history. Of the total treated, 50 were classified as progressive at time of penicillin treatment. No patient was treated with penicillin whose visual acuity was worse than 6/60 to 1/60 with correction. Only 13 of the 50 patients had prepenicillin treatment. The optic atrophy of 6 patients was classified as stationary at the time of penicillin treatment.

Favorable or unfavorable progress of each patient was determined by comparison of visual acuities and perimetric fields. Of the 50 patients whose optic atrophy was progressive at time of penicillin treatment, 32 showed favorable progress in a period of observation ranging from 4 months to 53 weeks. Of these 32 patients, 15 were treated by the first schedule. The optic atrophy of 10 patients continued to progress. Two of these patients were lost from observation, but 6 of the 8 now under observation were re-treated. Observation has not been sufficiently long to evaluate the effect of re-treatment in all of these. Penicillin treatment in 8 patients did not arrest the progress of optic atrophy. Only 2 of these patients were re-treated with the inclusion of fever therapy.

Of the six patients whose optic atrophy was stationary at time of penicillin treatment, all remained stationary after such treatment for a period ranging from 32 to 53 months. Since none showed unfavorable progress, re-treatment was administered to one patient only, and this was directed at paretic symptoms.

No correlation could be made between spinal fluid response, penicillin treatment, and the progress of the optic atrophy. It is apparent that the effect of penicillin was variable. Some patients did well after little therapy, others progressed unfavorably after much more therapy. The most satisfactory results were obtained in the six patients in the stationary group.

Ratio of gonorrhea to syphilis as occurring in the United States Navy. Robert W. Babione. Am J. Syph., Gonor. & Ven. Dis., 33: 243–262, May 1949.

In 1945 the Navy began reporting syphilis by stage of disease, thus affording the opportunity for comparing the incidence of gonorrhea with that of early syphilis. By this method the rates of acquisition of the 2 diseases at various ages could be more accurately compared. During that year, there were reported 107,138 new cases of gonorrhea and 12,135 cases of syphilis (all forms) giving a ratio of 8.9 to 1. Of the syphilis cases, 6,612 were reported as early syphilis, giving a gonorrhea/early syphilis ratio of 16.2 to 1. As with previous studies, it was noted that both ratios showed a downward trend with increasing age.

The age-specific ratios of gonorrhea to early syphilis were approximately 17 in age groups below 25 years and declined steadily to 8 in the age group of 40 to 44 years. Ratios were still lower in age groups over 45 years. The age-specific ratios for gonorrhea to all forms of syphilis were 14 to 12.5 below 20 years of age, 10.5 to 9.3 at ages of 20 to 24 and declined steadily to 0.9 in the age group of 45 to 49 years. Age-specific ratios for Negro men declined in a similar manner to those for white men but always at a lower level.

Because of this trend and the marked preponderance of young white men in the Naval population, the ratios shown are too high for application to civilian male populations. The most likely explanations for the trend would seem to be: (1) self-treatment, nonofficial treatment, or nonreporting of gonorrhea, to a greater degree in older groups who are more experienced, under more social pressure, and better off financially; (2) the development of some degree of immunity to gonorrhea on the part of those who frequently expose themselves. The first factor was at a minimum in the Navy. The second should virtually disappear with the application of early and effective chemotherapy of gonorrhea, and to the extent that this underlies the age-specific decline in ratio noted in 1945, that decline should diminish in the future.

Within the armed forces, changes in the future in the ratio of gonorrhea to syphilis may require an age adjustment, since the age distribution of men changes from time to time. This changing age composition affects both the gross rates of gonorrhea and syphilis and their ratio, and it should be taken into account when considering trends of venereal disease rates within the armed forces and when comparing these with other selected population groups.

Aureomycin treatment of acute gonorrhea in males. Harvey Shields Collins, Helen Trousdale, Thomas F. Kaiser, Francis C. Regan and Maxwell Finland. Am. J. Syph., Gonor. & Ven. Dis., 33: 263–269, May 1949.

The patients selected for treatment with aureomycin were males with active acute gonorrhea and with a purulent urethral discharge that was positive for gonococci both by smear and culture. Most of the patients had had one or more previous attacks of gonorrhea. Some had received sulfonamides without relief during the present attack, but no patient was chosen for aureomycin treatment if he had already received penicillin for the present attack.

For each patient, a culture of the urethral exudate was planted on suitable media and a smear of the exudate was stained and examined at the time of the initial visit. The patients were given the first dose to take at that time and a sufficient additional supply of the antibiotic to complete the course outlined. In some patients in whom treatment was continued for more than 1 day, the amount required for the first day was given at the first visit, and enough to complete the course was given on the following day after the patient was seen again. Patients were considered cured only if they became entirely free of symptoms and discharge and if their prostatic secretions showed very few, if any, cells and were negative for gonococci by both smear and culture.

Considering all the 122 patients in whom there was any opportunity for follow-up after completion of the treatment, there were 16 failures. This gave a cure rate of 87 percent. The 16 failures included 7 patients who probably had reinfections since they had satisfied the clinical and laboratory criteria of cure for several days.

A comparison of the results obtained with the different dosage schedules suggests that a total of 2.5 gm. or more must be given over a period of 36 hours or longer in order to achieve the optimum cure rate. There were no toxic effects noted in any of the patients.

The clinical and bacteriologic results in the present study seem to justify the conclusion that oral aureomycin, in the dosage used, is a highly effective therapy for acute gonorrhea in males. The overall results, however, are definitely inferior to those obtained in the clinic with a single intramuscular dose of 300,000 units crystalline penicillin in a delaying agent such as beeswax and peanut oil. Weight for weight, aureomycin is much less active against gonococci in vitro than penicillin, but is much more active than streptomycin, bacitracin, polymyxin D, polymyxin B, and sulfadiazine.

AM. J. TROP. MED., BALTIMORE

A five day peroral treatment of yaws with STB, a new trivalent arsenical. Ernst A. H. Friedheim. 29: 185–188, Mar. 1949.

AM. PRACT., PHILADELPHIA

The treatment of acute proctologic conditions. [V. D.] Emil Granet. 3 : 533–538, May 1949.

The triad of urethritis, conjunctivitis and arthritis. Aaron M. Lefkovits. 3 : 619–625, June 1949.

The diagnosis of syphilis confused by penicillin therapy of other diseases. Thomas H. Sternberg and Paul Le Van. 3 : 720–722, Aug. 1949.

ANN. INT. MED., LANCASTER

Clinical angiocardiography : a critical analysis of the indications and findings. Charles T. Dotter and Israel Steinberg. 30 : 1104–1125, June 1949.

Gonococcal arthritis : a study of 202 patients treated with penicillin, sulfonamides or fever therapy. Jay A. Robinson, Harold L. Hirsh, William W. Zeller and Harry F. Dowling. 30 : 1212–1223. June 1949.

Observations on primary coccidioidomycosis. Ashton B. Taylor and Allan K. Briney. 30 : 1224–1235, June 1949.

Penicillin and penicillin-malaria in the treatment of tabes dorsalis. Henry Packer and Y. T. Wong. 31 : 96–104, July 1949.

ARCH. DERMAT. & SYPH., CHICAGO

A case for diagnosis (Syphiloderm?). H. D. Pocock, Jr. Society Transactions-Cleveland. 58 : 557–559, Nov. 1948.

Treatment of early syphilis with small doses of crude penicillin. A. E. Walker and Manly Utterback. 59 : 277–283, Mar. 1949.

Keratosis blennorrhagica. Response to streptomycin : report of a case. Robert G. Thompson, Claude B. White and Howard Hailey. 59 : 284–292, Mar. 1949.

*Quantitative serologic titer in post-treatment observation of early syphilis treated with penicillin. Milton H. Gustafson and Jack H. Bowen. 59 : 303–307, Mar. 1949.

Treatment of early syphilis with penicillin injection in oil and wax U. S. P. Report of one hundred and fifty-three cases. Louis Chargin, Nathan Sobel, Charles Rein and Theodore Rosenthal. 59 : 595–605, June 1949.

Quantitative serologic titer in post-treatment observation of early syphilis treated with penicillin. Milton H. Gustafson and Jack H. Bowen. Arch. Dermat. & Syph., 59: 303–307, Mar. 1949.

From a total of 700 patients, 117, all with early syphilis, were selected for study entirely on the basis of continuous and regular monthly determination of the serologic reaction of the blood for 12 months or longer. Because this group was studied only for the quantitative serologic response to penicillin therapy of early syphilis, the contents of this report cannot be considered indicative of the efficacy of penicillin therapy.

By the end of 1 year, 71 patients became seronegative and clinically well; 46 patients had either a serologic or a seroclinical relapse. The serologic titer became negative in 56 percent within 3 months and in 91 percent within 6 months after treatment of the 71 patients who were considered clinically well and seronegative. Of the 46 patients who had relapses, 69 percent had relapses within 6 months and 80 percent within 9 months after treatment. In these patients, a gradual rise in the serologic titer preceded the relapse.

There was a fluctuation in the quantitative titer after the achievement of negativity in 33 percent of the well patients examined. The fluctuation varied from 1 to 3 Kahn units. A characteristic feature was the return to permanent negativity within 2 months. Paralleling this fluctuation in titer in the well group, 30 percent of the relapsed group attained temporary negativity. This drop to negativity was usually sharp, and then within 2 months the titer was again high or was increasing steadily.

The writers conclude that in cases of the penicillin treatment complicating pregnancy, the quantitative serologic titer serves one of its most valuable roles. A monthly or bimonthly quantitative test on the newborn will indicate whether the positive reaction of the cord blood, or the serologic titer at birth, was due to an active syphilitic infection or was attributable to the transfer of the maternal reagins through the placenta to the fetal circulation.

A single negative serologic titer during the early months of follow-up observation is not of great prognostic significance, for it has been seen that this occurred in approximately one-third of the patients in the group with relapses.

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Aureomycin and other antibiotics. W. Schweisheimer. 122 : 164–165, 190, Apr. 1949.

STATISTICS

First Admissions to Mental Hospitals[1] for All Psychoses and for Psychoses Due to Syphilis, United States, 1922, 1933–1947

Year	Number of first admissions				Percent of all psychoses due to syphilis	Rates per 100,000 population			
	All psychoses	Paresis	Other syphilis of the central nervous system	Total psychoses due to syphilis		All psychoses	Paresis	Other syphilis of the central nervous system	Total psychoses due to syphilis
1922	64, 689	6, 260	892	7, 152	11. 1	58. 8	5. 7	0. 8	6. 5
1933	80, 974	6, 889	1, 429	8, 318	10. 3	64. 5	5. 5	1. 1	6. 6
1934	80, 575	6, 869	1, 428	8, 297	10. 3	63. 8	5. 4	1. 1	6. 6
1935	83, 943	6, 974	1, 432	8, 406	10. 0	66. 0	5. 5	1. 1	6. 6
1936	88, 259	7, 070	1, 343	8, 413	9. 5	68. 9	5. 5	1. 0	6. 6
1937	89, 858	6, 918	1, 357	8, 275	9. 2	69. 8	5. 4	1. 1	6. 4
1938	89, 461	6, 962	1, 255	8, 217	9. 2	68. 9	5. 4	1. 0	6. 3
1939	90, 143	7, 261	1, 364	8, 625	9. 6	68. 9	5. 5	1. 0	6. 6
1940	87, 592	6, 558	1, 136	7, 694	8. 8	66. 5	5. 0	. 9	5. 8
1941	94, 176	6, 938	1, 145	8, 083	8. 6	70. 8	5. 2	. 9	6. 1
1942	94, 310	6, 786	1, 139	7, 925	8. 4	70. 5	5. 1	. 9	5. 9
1943	92, 126	6, 316	968	7, 284	7. 9	68. 8	4. 7	. 7	5. 4
1944	93, 821	6, 179	889	7, 068	7. 5	70. 8	4. 7	. 7	5. 3
1945	95, 119	6, 008	889	6, 897	7. 3	72. 0	4. 6	. 7	5. 2
1946	101, 444	5, 746	801	6, 547	6. 5	72. 5	4. 1	. 6	4. 7
1947	99, 511	5, 247	743	5, 990	6. 0	69. 4	3. 7	. 5	4. 2

[1] Excluding admissions to Veterans Administration hospitals.

USPHS—Division of Venereal Diseases, Office of Statistics, 9/16/49 (MJM-FFD)mjm.

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The JOURNAL *of* VENEREAL DISEASE INFORMATION

Volume 30 December 1949 Number 12

EDITORIAL

Contact Investigation of Syphilis 339

ORIGINAL ARTICLES

Factors Affecting the Results of Interviewing for Contacts 341
J. Wallace Rion, *Health Program Officer*
Sidney Abraham, *Health Program Analyst*

Observation of the Kolmer Complement-Fixation Test and the VDRL Spinal Fluid Test 347
Frank M. Victor, B. S.
Charles A. Hunter, Ph. D.

Penicillin Treatment of Early Syphilis—First Four Patients After Six Years 350
J. F. Mahoney, *Medical Director*
R. C. Arnold, *Senior Surgeon*
Ad Harris, *Serologist*

CURRENT NOTES AND REPORTS 356

CURRENT LITERATURE 359

STATISTICS

Contact Investigation Indices, January 1944–December 1948 . . . 362

INDEX 364

FEDERAL SECURITY AGENCY
Public Health Service

Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in the JOURNAL OF VENEREAL DISEASE INFORMATION, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the JOURNAL, and should be presented on separate sheets, rather than within text material.

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Chief, Division of Venereal Disease

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Editorial

Contact Investigation of Syphilis

Contact investigation discovers approximately 25 percent of the primary and secondary syphilis, 29 percent of the early latent syphilis, 25 percent of the congenital syphilis, and 18 percent of the late syphilis now being diagnosed in clinics throughout the United States. A new case of syphilis is diagnosed for every 2 contacts of early lesion syphilis examined, whereas only 1 out of 20 persons seeking diagnosis of their own accord is diagnosed as a new case of syphilis. Contact investigation is a selective process that brings to examination only persons exposed to known cases of syphilis.

In recent years contact investigation of primary and secondary syphilis has been stimulated by the publication of indices designed to evaluate the process. These indices for a 4-year period are given in the section under "Statistics" at the back of this issue of the Journal. It will be noted that there has been a gradual, steady improvement in the accomplishment of contact investigation over the years. On a "per patient" basis, the number of contacts reported has increased 51 percent; the contacts identified as infected, 62 percent; the contacts brought to treatment, 94 percent; and the new cases of syphilis with open lesions, 89 percent. Health departments are to be congratulated on such a remarkable record of progress. It is hoped that this record of progress will continue. With the decline in open lesion syphilis coming to clinics, it becomes more important than ever that each case of early infectious syphilis be interviewed for contacts immediately and the contacts examined at the earliest possible moment. Thus the chains of infection can be snapped more quickly and the incidence further reduced.

Most health departments are convinced of the importance of this process and have emphasized the interview for contacts as a "must" in patient management. Moreover, it is recognized that the interviewer must have a fundamental grasp of the process and a certain amount of skill in interviewing. It has been demonstrated in several areas that with proper explanation of the purpose and methods and a brief course in interviewing technics, newly trained workers can average over three contacts per patient.

It should be remembered that contact investigation discovers more cases of latent syphilis than it does of early lesion syphilis. Possibly because of the continued publication of the indices on primary and secondary syphilis some workers have felt that contact investigation is a process limited to early lesion syphilis. This is not so. All newly diagnosed cases of syphilis are potential candidates for contact interviewing. With few exceptions and regardless of the stage of syphilis, the spouse should be examined. Children of mothers with syphilis should be examined if born since the probable date of acquiring syphilis. In case of doubt examine the child. The later the stage of syphilis in the mother the more imperative the need for examination of the children. Moreover, mothers and all siblings of congenital syphilis cases should be examined without delay.

In a recent editorial, we commented on the continued high level of morbidity reporting of congenital syphilis. One of the methods of finding congenital syphilis is familial contact investigation. In fact, contact investigation should be the ideal method of finding it. It is surprising that only approximately 25 percent is found through this process. In a study of the medical history of newly discovered congenital syphilis it was found that in many instances the mother had been treated for syphilis but the child had not been examined. This is an absolute failure of public health. All children of women with syphilis should be examined for syphilis unless the known duration of the disease contraindicates it.

THEODORE J. BAUER, *Medical Director*
Chief, Division of Venereal Disease

Factors Affecting the Results of Interviewing for Contacts[1]

J. Wallace Rion, Health Program Officer, and Sidney Abraham, Health Program Analyst, United States Public Health Service

Successful interviewing is a contributing factor of major importance to efficient contact investigation. A previous study (*1*) showed that there is a tremendous variation between health departments in the degree to which interviewers succeed in obtaining the names of sex contacts. The degree of success is measured objectively by the contact index (the average number of contacts named by patients). At the present time, the degree of success in contact interviewing is the most important factor contributing to variations in the overall results of contact investigation (the number of cases of syphilis identified through contact investigation per new case of syphilis diagnosed) (*1*, *2*). In other words, areas with high contact indices consistently show the best results in the process of contact investigation.

Since, at the present time, the greatest improvement in contact investigation can be achieved by an improvement in contact interviewing, the present study was undertaken to discover whether the variations in contact indices can be attributed to factors over which the health department can exercise some control, or whether they are inherent in the types of patients in different areas.

The factors influencing the number of contacts obtained can be classified in two broad fields: (1) those deriving from the behavior and personality of the patients being interviewed; and (2) those deriving from the particular interviewing situation (interviewer, interview environment, etc.). Differences in the actual number of persons with whom patients have had intercourse, in the ability of patients to recall the information needed to initiate a contact investigation (which may in turn be due to differences in mental ability or to differences in patterns of promiscuity), and in the degree to which patients are willing to cooperate in revealing contact information, all play a part in determining the number of contacts named. Likewise, the general atmosphere and attitude of the health facilities and personnel and the skill of the interviewer in obtaining cooperation and information are important in determining the number of contacts named.

The tremendous variation in the number of contacts named by different patients is well known to anyone who has interviewed for contacts. At one end of the scale there are some patients who name an almost unlimited number and at the other end are patients who admit no sexual contact. It has been felt in some quarters that equally sizeable variations might be found between groups of patients, particularly between males and females or whites and Negroes. If such large variations do exist, they would invalidate the comparison of contact indices between areas where the race and sex composition of the patient population are dissimilar.

A study of the number of contacts named by patients, grouped by race and sex and interviewed in various situations, should indicate whether these differences in contact indices can be attributed more to differences in the characteristics of the patients interviewed or more to differences in the interviewing situation. Such a study was made between September 1946 and December 1947 at the rapid treatment centers and clinics of the following States: South Carolina, Alabama, Missouri, Arkansas, Georgia, West Virginia, Oklahoma, Nebraska, New Mexico, and Virginia. A card, indicating the race and sex of the patient and the total number of sex contacts named, was prepared for each case of previously untreated primary and secondary syphilis admitted for treatment during the period of the study. In addition, certain of the treatment centers secured other data regarding the patient being interviewed, which was also entered on the study card. All information was secured at the time of the contact interview. The count of sex contacts obtained includes the unduplicated total of all reinterviews if the patient was interviewed more than once. A total of 1,968 patients with primary or secondary syphilis was included in this study, of whom 461 were white males, 318 were white females, 608 were Negro males, and 581 were Negro females.

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[1] From the Division of Venereal Disease, U. S. Public Health Service.

Variations Caused by Differences in Interviewing

Table 1 shows the over-all results of the analysis of the data. It is apparent from this table that there is a great deal more variation between the contact indices obtained in different areas than there is in contact indices obtained from the interview of groups of patients of different race or sex. It would seem safe to assume, then, that the variations in contact indices reported by different areas can be attributed more to differences in interviewing situations than to differences in types of patients, as classified in this study.

The same point can be shown in other ways. When the 10 areas are divided into two classes—those having an over-all contact index greater than 3.0 (identified as class A areas) and those with an index of 3.0 or less (class B areas)—the average contact index for class A areas is 4.10, and that for class B areas is 2.59, a difference of 1.51 contacts. If these areas had interviewed the same proportion in each sex-race category (a condition that can be created by simple weighting), the indices would be 4.00 and 2.59, respectively, which is still a difference of 1.41 contacts. Figure 1 indicates that the differences in contact indices found between class A areas and class B areas are consistent within each of the race-sex categories. Thus, the class A areas are superior in over-all accomplishment not because of the type of patient interviewed but because their interviewers secured the names of more contacts per patient from all categories of patients.

Table 1 also presents the contact indices obtained in each center from white male, white female, Negro male, and Negro female patients (this study was limited to whites and Negroes; unknown and other races were excluded). The variation from area to area for each group of patients is immediately apparent. Contact indices for white males range from 1.50 in area 1 to 3.65 in area 10; for white females, from 1.79 in area 2 to 4.71 in area 9; for Negro males, from

Table 1.—***Number of contacts named per primary and secondary syphilis patient admitted to rapid treatment centers and clinics, by race and sex***

Area	White				Negro			
	Male		Female		Male		Female	
	Number of patients	Contact index	Number of patients	Contact index	Number of patients	Contact index	Number of patients	Contact index
1	4	1.50	10	2.00	70	2.33	76	2.00
2	58	2.02	33	1.79	12	2.25	10	2.30
3	14	1.93	13	2.69	22	2.27	8	2.13
4	82	2.41	49	2.29	58	2.64	63	2.40
5	15	1.60	8	2.88	86	3.20	109	2.83
6	154	2.58	116	3.71	21	2.41	21	2.90
7	20	2.45	8	3.50	80	3.81	65	3.09
8	31	2.97	42	3.86	57	3.40	66	3.91
9	43	3.02	14	4.71	150	4.37	120	5.05
10	40	3.65	25	4.60	52	6.02	43	4.42

2.25 in area 2 to 6.02 in area 10; and for Negro females, from 2.00 in area 1 to 5.05 in area 9. In all these comparisons, the variations between areas were found to be statistically significant at the 1-percent level. Careful examination fails to reveal any regional pattern in these differences.

Such differences between areas, which are significant for all race-sex groups, are probably due to differences in the interviewing situation in different areas. A patient who has received courteous and considerate treatment from health department personnel (clerks, nurses, and doctors) is more likely to cooperate in the contact interview. A treatment center which has established a community reputation for such courteous and considerate treatment has set the stage for a successful contact interview. An interview room which provides comfort and privacy makes the interviewer's job easier. The personality of

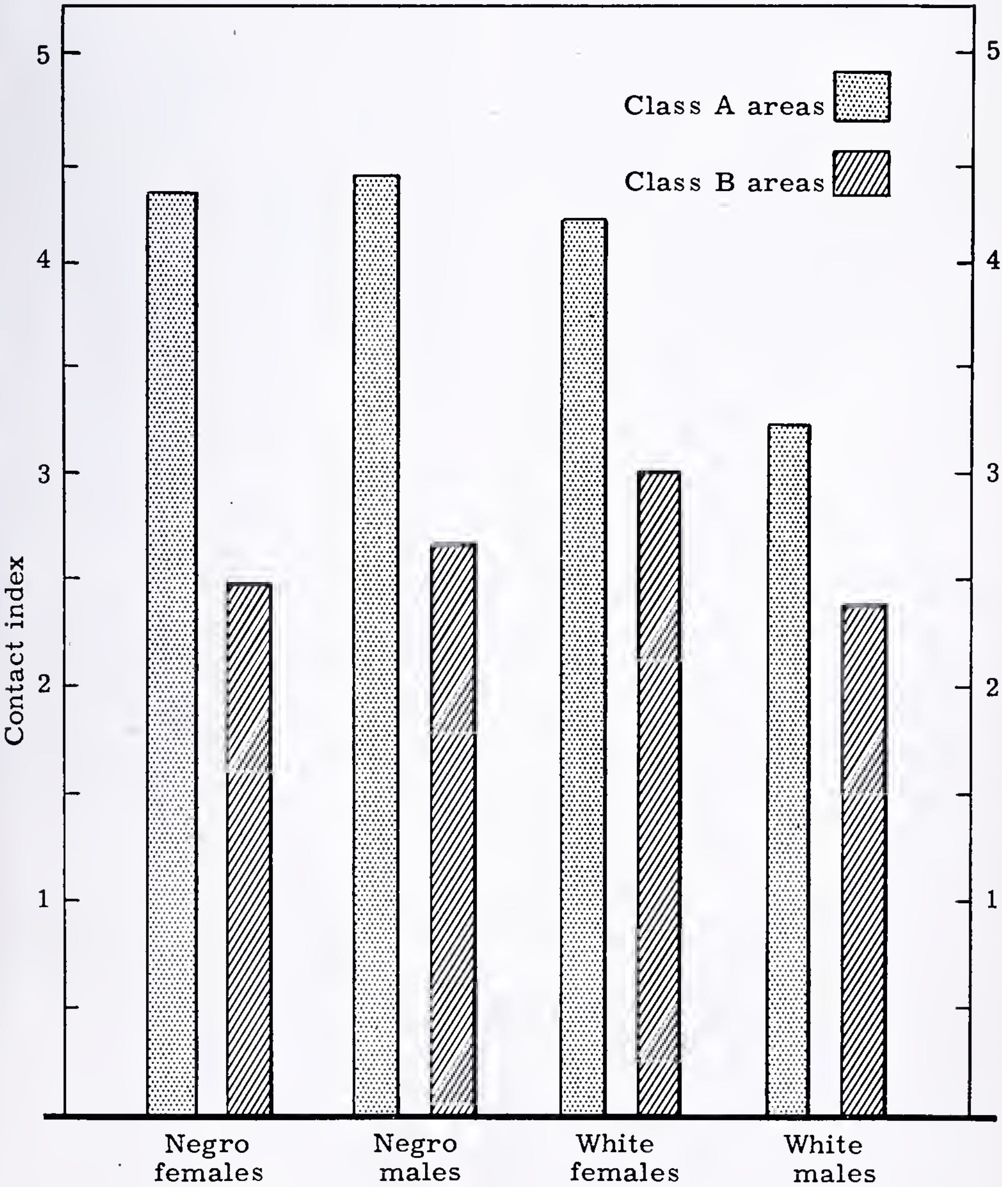

FIGURE 1.—Contact indices obtained in class A areas and in Class B areas, by race and sex.

the interviewer, the training he has received, and the methods he uses are important in determining the results he achieves.

The data from the present study indicate that variations in these interviewing conditions account for most of the variations in contact indices in these areas, but the data do not show the relative importance of each interviewing condition in determining the present reported variations.

Variations Caused by Race-Sex Differences

The figures presented in this study concern the number of sex contacts *named* by patients, and are different from the actual number of persons with whom the patients have had intercourse during the period covered by the contact interview to the extent that some patients withhold information. Differences in contact indices between groups of patients thus reflect differences in degree of cooperation as well as differences in the actual number of sex partners. Also, some patients cannot recall the information needed to initiate a contact investigation; patients with poor memories and patients who pick up their sex partners so casually that they fail to learn even their first names obviously cannot name all of their sex partners.

Figure 2 and table 2 show an analysis of the number of contacts named by patients in each race-sex group. The general shape of the distribution for each group is the same—a concentration of patients naming 1, 2, or 3 contacts, with a tapering off in the number of patients naming more contacts. More than 12 contacts were reported by patients in only 2 groups—white females and Negro males. In each group, the number of contacts most frequently reported was 2, except in the white female group (in which the modal number was 1 contact). The white female patients had the greatest variation. The largest number of contacts reported by a single patient (a white female) was 34.

In comparing the number of contacts named by white males with the number named by white females, we find that the white females had a contact index of 3.31 as against a white male contact index of 2.57—a difference of 0.74. This difference was statistically significant (see statistical appendix). The contact index for females was higher, in spite of a larger percentage of patients reporting less than two contacts, because of the higher percentage of females reporting more than seven contacts.

In making the same comparison between white males and Negro males, we find that Negro males had a contact index of 3.60 as against a white male contact index of 2.57—a difference of 1.03. This difference was statistically significant (see statistical appendix). A smaller percentage of Negro males named less than two contacts, and a higher percentage named more than seven contacts.

Table 2.—*Averages and distributions of contacts obtained, by race and sex of patient*

	White		Negro	
	Male	Female	Male	Female
Number of patients	461	318	608	581
Contact index	2.57	3.31	3.60	3.39
Modal number of contacts reported	2	1	2	2
Greatest number of contacts named by an individual patient	12	34	16	11
Percentage of patients naming less than two contacts	28.6	33.0	15.0	20.5
Percentage naming 6 or more	6.5	15.4	16.8	16.2
Percentage naming 7 or more	3.9	11.0	10.0	8.1
Percentage naming 8 or more	2.0	8.8	4.8	4.0
Percentage naming 9 or more	1.1	6.6	3.3	2.8
Percentage naming 10 or more	1.1	4.7	2.0	1.2
Measure of variation [1]	70	101	64	62

[1] Coefficient of variation.

PERCENT DISTRIBUTION OF NUMBER OF CONTACTS OBTAINED PER PATIENT BY COLOR AND SEX

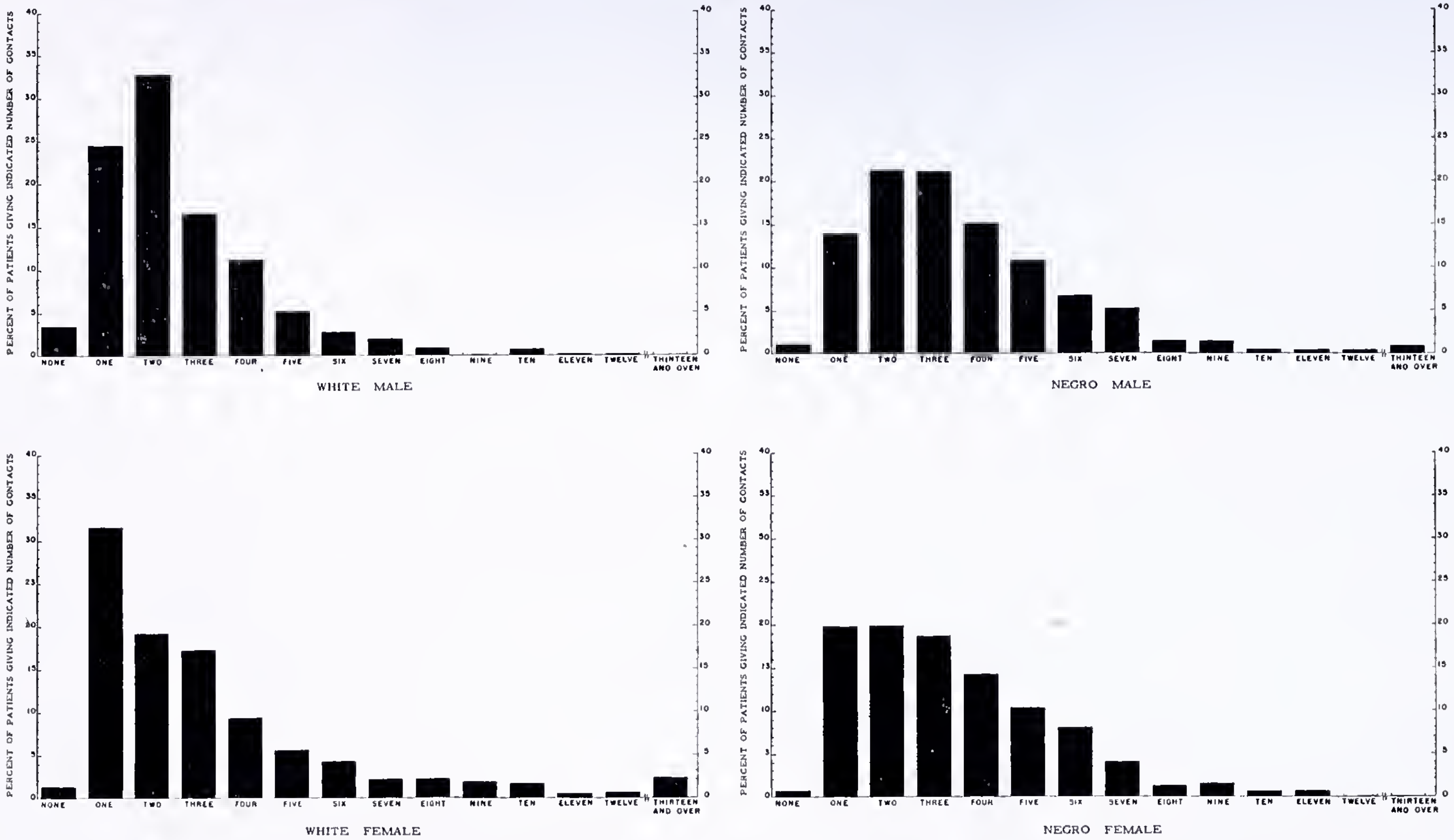

FIGURE 2.—Contacts obtained through health department interview of primary and secondary syphilis patients in clinics and rapid treatment centers (special study, "Patient Response to Contact Interview," 10 areas, in the period September 1946 to December 1947).

Negro females had a contact index of 3.39 as against a white female contact index of 3.31. This difference of 0.08 was not statistically significant (see statistical appendix). A smaller percentage of Negro females named less than two contacts, and a smaller percentage named more than seven contacts.

The Negro male contact index of 3.60 was 0.21 larger than the contact index for Negro females, 3.39. This difference was not statistically significant (see statistical appendix). A smaller percentage of Negro males named less than two contacts, and a higher percentage named more than seven contacts.

In summary, the material analyzed indicates that, while there are some differences in the pattern of contact reporting among the four groups, the contact indices for three of them (white females, Negro males, Negro females) are substantially the same. The contact index for white males is lower than the others by from 0.74 to 1.03 contacts.

A more detailed analysis, controlling for the factors of age, amount of schooling, marital status, and rural-urban residence, gives substantially the same results (see statistical appendix).

Summary

A study was made in 10 areas between September 1946 and December 1947 of the number of contacts named by 1,968 patients with primary or secondary syphilis (461 white males, 318 white females, 608 Negro males, 581 Negro females). This study was undertaken in order to discover whether the variations in contact indices are associated with factors over which the health department can exercise some control, or whether the variations are associated with differences in the types of patients available for interview.

Analysis of the data revealed that interviewing differences were the main source of variation, rather than differences in the type of patient available for interview.

Further study is necessary to determine the interviewing conditions that produce the best results.

Statistical Appendix

Race-Sex Differences

An analysis was made comparing race-sex variance between areas with race-sex variance within areas. The analysis of variance technic was modified (*3*) to account for the disproportionate number of patients interviewed in those subgroups within areas. Table 3 shows the comparison of contact indices between races and sex groups.

Table 3.—*Comparison of contact indices between race and sex groups*

Comparison of contact indices by race-sex groups		Difference in contact indices
White:		
Males 2.57	Females 3.31	[1] 0.74
Negro:		
Males 3.60	Females 3.39	[2] 0.21
Males:		
White 2.57	Negro 3.60	[1] 1.03
Females:		
White 3.31	Negro 3.39	[2] 0.08

[1] Statistically significant at the 1-percent level.
[2] Not statistically significant.

Influence of Other Factors

With 7 factors, each split in dichotomous fashion, and with 10 areas, the data would be subdivided into 1,280 categories (2^7 x 10), one of which would be, for example, the contact index for the category of patients in a given area who were white, male, under 22 years of age, single, from a rural community, who had less than 8 years of schooling, and who had not moved within the past 6 months. Having only some 1,500 patients who might be placed in these 1,280 categories, it became necessary to devise a scheme of analysis which would make most effective use of these limited data.

Since no valid comparisons could be made between transients and nontransients, due to the small number of transients, the latter were excluded, and the study then covered stable patients, those who had not moved within the 6-month period prior to interview. Also excluded were the unknowns (unknown sex, race, age, etc.) and those persons still in school. Median values for age and for school years completed were used in making the dichotomous split between "under 22 years" and "22 years and older" and between "under 8 years of schooling" and "8 years and more of schooling," since this tended to maximize the number of possible group comparisons. It was decided to omit from analysis any group having less than 5 patients, since contact indices computed for such a small group would be unreliable. Instead of considering each of the 10 areas, they were divided into 2 classes on the basis of their over-all contact indices. Those with indices over 3.0 were put into class A, and those with 3.0 or less into class B. The contact indices for these 2 classes were 2.6 for class B and 4.1 for class A. The question was then—do classes A and B differ by 1.5 contacts because they have different types of patients to interview? Or, put another way—do interviewers in class A obtain more contacts per patient than do the interviewers in class B even when they interview the same type of patients?

The analysis by this procedure revealed that the areas in class A maintained their superiority, on the average, in approximately 75 percent of the groups compared. For example, the contact index for class A was 4.0 and for class B was 2.9 when the interviewing was confined to the following particular group: Negro males, under 22 years of age, single, with 8 or more school years completed, and residing in an urban area. This type of comparison was made for other groups.

Potentially, there were 64 possible comparisons that could be made; however, due to the exclusion of indices based on less than 5 patients, only 38 comparisons were possible. Of the 38 comparisons, class A contact indices exceeded class B contact indices in 28 instances, and the average difference was about one contact more for the class A areas. Thus, those areas achieving high contact indices did so irrespective of the categories of patients interviewed.

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Observation of the Kolmer Complement-Fixation Test and the VDRL Spinal Fluid Test[1]

Frank M. Victor, B. S.,[2] and Charles A. Hunter, Ph. D.[3]

The spinal fluid specimens received in the public health laboratories of Kansas are routinely tested with the Kolmer complement-fixation test, the colloidal gold test, and the quantitative estimation of total protein. However, conflicting results are frequently obtained using these tests, the most frequent disagreement being the obtaining of positive Kolmer reactions with normal colloidal gold reactions and normal total protein values. In view of such disagreement, a need exists for an additional serologic test for syphilis.

In selecting an additional serologic

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[1] From the Division of Public Health Laboratories, Kansas State Board of Health, Topeka, Kansas.

[2] Principal Serologist.

[3] Director of Laboratories.

test, the following features were desired: (1) satisfactory sensitivity and specificity, as compared with other accepted tests; (2) easy readability; (3) a narrow range of doubtful and weak positive reactions. The VDRL spinal fluid test employing cardiolipin-lecithin antigen, as described by Rosenberg and associates (*1*), was found by them to give results comparable to the Kahn, Kline, and Kolmer tests and to be more sensitive than the Eagle flocculation test. This test, which is also reported as positive or negative, with no doubtful reaction, was therefore selected as an additional serologic test on spinal fluids.

The Kolmer test used in this laboratory is described in "Technics of Serodiagnostic Tests for Syphilis," published by the United States Public Health Service in 1944 (*2*); however, the improved Kolmer antigen (*3*) is used. The VDRL test is used as described by the authors. The antigen for this study was provided by the United States Venereal Disease Research Laboratory.

The spinal fluids received are not all clear, many being contaminated with bacteria and/or blood. It has been the policy to test all specimens received and to report those that are visibly turbid (whether due to bacteria or blood) with a note that the results cannot be considered in this study, since the procedure for the VDRL test states that "Spinal fluids which are visibly contaminated or contain gross blood are unsatisfactory for testing." The spinal fluids are received without data as to the clinical status of the patient; this study therefore gives no information as to the specificity or sensitivity of the VDRL test, except by comparison with the Kolmer test.

The spinal fluids included in this study were received during the period December 1, 1948, to July 1, 1949. A total of 503 specimens was examined by both tests. This number does not represent the entire total received during that period, however, as many were insufficient in quantity for the additional test, and the visibly turbid specimens were excluded.

The findings are listed in tabular form. Table 1 gives the number of positive, doubtful, and negative reactions obtained with each test. It will be noted that the Kolmer test gave a slightly higher percent of reactions than did the VDRL test.

Table 1.—***Serologic results obtained on 503 spinal fluids, using the Kolmer complement-fixation test and the VDRL spinal fluid test***

Test	Serologic results					
	Positive		Doubtful		Negative	
	Number	Percent	Number	Percent	Number	Percent
Kolmer	118	23.46	11	2.19	374	74.35
VDRL	111	22.07	----	----	392	77.93

Table 2 gives a direct comparison of the reactions. Complete disagreement was encountered in 14 specimens, that is, positive with one test and negative with the other. Partial agreement was found in 11 specimens.

Table 3 has been included to give the Kolmer reading, as well as the colloidal gold reactions and total protein reactions of the specimens that show partial or complete disagreement. A total of 25 specimens is included in this table, which shows that the greatest disagreement is found within weak reactions; actually only 5 specimens gave negative VDRL results, as compared to 4+ Kolmer reactions. The disagreement was largely in the doubtful Kolmer and negative VDRL reactions.

Table 2.—*Comparison of serologic results obtained, using the Kolmer complement-fixation test and the VDRL spinal fluid test*

	Results					
	Agreement		Partial agreement		Disagreement	
Number of specimens tested	106	372	3	8	12	2
Kolmer VDRL	Positive Positive	Negative Negative	Doubtful Positive	Doubtful Negative	Positive Negative	Negative Positive

Table 3.—*Results of examination of 25 spinal fluids showing partial or complete disagreement between the Kolmer and VDRL tests*

Specimen No.	Colloidal gold reaction	Total protein reaction (mg. per 100 ml.)	Kolmer complement-fixation test	VDRL spinal fluid test
80970	0111100000	30	4 Positive	Negative.
104883	1221100000	45	4 Positive	Negative.
49220	0012110000	45	4 Positive	Negative.
100084	0011100000	50	4 Positive	Negative.
100142	0000000000	25	4 Positive	Negative.
89327	1112210000	40	3 Positive	Negative.
51570	0000000000	15	3 Positive	Negative.
114735	5443210000	55	2 Positive	Negative.
71203	0000000000	40	2 Positive	Negative.
48877	0000000000	25	2 Positive	Negative.
96682	0000000000	50	1 Positive	Negative.
56284	0000000000	35	1 Positive	Negative.
50588	0001221000	180	±Doubtful	Negative.
86995	0002210000	40	±Doubtful	Negative.
84764	5554322100	30	±Doubtful	Negative.
85888	0000000000	30	±Doubtful	Negative.
100885	0000000000	25	±Doubtful	Negative.
61644	0000000000	20	±Doubtful	Negative.
78030	0000000000	20	±Doubtful	Negative.
51116	0000000000	20	±Doubtful	Negative.
73400	1122110000	70	Negative	Positive.
76513	0000000000	20	Negative	Positive.
69633	0000000000	30	±Doubtful	Positive.
70256	0000000000	20	±Doubtful	Positive.
94398	0000000000	25	±Doubtful	Positive.

Summary

1. This paper presents the results obtained with the Kolmer and VDRL tests on spinal fluids.

2. The VDRL test is simple to perform and easy to read.

3. The data presented give no criteria as to specificity or sensitivity of the VDRL test, except by comparison with the Kolmer test, since the clinical status of the patients is unknown.

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Penicillin Treatment of Early Syphilis—First Four Patients After Six Years[1]

J. F. Mahoney, Medical Director, R. C. Arnold, Senior Surgeon, and [illegible]d Harris,
Serologist, United States Public Health Service

More than 6 years have passed since the then newly developed antibiotic, penicillin, was first employed in the management of early syphilis. The preliminary report (*1*) was presented in October 1943 and was based upon the findings in a group of four patients. All of this group have been observed, in a more or less satisfactory manner, until the present. In the interest of medical history, and as a means of testing the validity of some of the inferences in the original publication, it is desired to place on record the details of the posttreatment observations of the four patients.

The members of the group were young males. Each displayed a reasonably characteristic lesion of primary syphilis, the duration of the lesion not exceeding 10 days in any. In each instance, *Treponema pallidum* was demonstrated by a darkfield examination of secretion from the lesion. Varying degrees of serologic reaction were present at the time of the inauguration of treatment, but all patients were well into the seropositive phase at the completion of therapy. There were no histories of previous syphilitic infections.

The serologic routine has remained the same for follow-up as it had been for diagnosis. A battery of accredited American tests has been employed, and quantitations have been carried out with two methods, Kahn and Mazzini. Quantitation in the complement-fixation test was discontinued early in the period of posttreatment observation. All of these procedures have been maintained, as far as possible, at the same level of reactivity, and all have been performed in strict accordance with the technical dictates of the several originators. In the detection of evidence of treatment failure, a reasonably complete medical examination was conducted whenever possible, and reliance was placed on the serologic tests on the basis of the strong probability that serologic evidence of relapse will precede, or at least accompany, a clinical relapse.

Treatment consisted of the intramuscular administration of 25,000 units of an amorphous penicillin preparation at 4-hour intervals for a total of 48 injections. The routine required 1.2 million units of the antibiotic and a treatment period of 8 days.

No additional treatment for syphilis was received by any of the patients except that which will be mentioned in connection with patient 4.

Follow-up in three members of the group was not as regular as might be desired. In a measure this was due to the fact that the patients were seamen and that the period of observation included two of the war years, during which the activities of most young males were not left to their personal discretion. However, all the members of the group were brought under observation recently. As the findings at the beginning of the lapsed periods were the same as those displayed upon resumption of observation, it seems reasonable to assume that the interim findings would have been of the same general character.

Spinal fluid examinations have been made of material from each patient without any evidence of abnormal changes.

Chart 1 displays all data concerned with the diagnosis, treatment, and posttreatment observation of the first patient treated with penicillin. At the completion of therapy on the eighth day, all serologic tests were positive. By the eightieth day, all serologic tests, with the exception

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[1] From the Venereal Disease Research Laboratory, U. S. Marine Hospital, Staten Island 4, N. Y., Senior Surgeon R. C. Arnold, Director.

Chart 1

Patient 1: L. W., white, male, 27 years old.
History: Treated for gonorrhea in 1935—no relapse.
Negative serology April 15, 1943.
Incubation—23 days.
Chancre: Penile, darkfield-positive.
Diagnosis: Primary syphilis—9 days.
Treatment: 25,000 units penicillin every 4 hours for 48 injections; date begun: June 21, 1943.
Reaction: Transitory macular rash over torso and thighs.
Temperature: 38.5° C.
7 days—ulcer healed.

Period of observation (days)	Qualitative methods							Quantitative methods		
	Kline exclusion precipitation	Mazzini flocculation	Kline diagnostic precipitation	Kahn standard precipitation	Hinton flocculation	Eagle flocculation	Kolmer simplified complement-fixation	Mazzini flocculation	Kahn precipitation	*Units*
0	—	4	—	4	P	P	4	4 4 4 2 1 — — —	4 4 4 2 ± — — —	32
1	—	4	—	4	P	P	4	4 4 4 2 1 — — —	4 4 4 2 ± — — —	32
9	4	4	4	4	P	P	4	4 4 4 4 2 — — —	4 4 4 4 1 — — —	32
23	—	4	—	3	P	P	4	4 3 2 — — — — —	4 4 1 — — — — —	8
30	4	4	3	3	P	—	4	4 4 4 2 — — — —	4 4 3 1 — — — —	16
37	4	4	1D	3	D	—	3	4 4 2 1 — — — —	4 1 — — — — — —	4
44	3	4	—	1D	—	—	4	4 3 2 — — — — —	4 ± — — — — — —	4
[illegible]	1D	4	—	—	—	—	4	4 2 — — — —	1 — — — — —	<1
[illegible]	1D	4	—	—	—	—	—	4 3 — — — —	1 — — — — —	<1
[illegible]5	2	2D	—	—	—	—	—	2 1 — — — —	— — — — — —	—
[illegible]2	1D	2D	—	—	—	—	—	2 1 — — — —	— — — — — —	—
80	—	2D	—	—	—	—	—	2 ± — — — —	± — — — — —	—
86	—	2D	—	—	—	—	—	2 — — —	— — —	—
93	—	1D	—	—	—	—	—	1 — — —		—
101	±D	1D	—	—	—	—	—	1 — — —		—
108	±D	1D	—	—	—	—	—	1 — — —		—
114	—	1D	—	—	—	—	—			
121	—	—	—	—	—	—	—			
128	±D	—	—	—	—	—	—			
135	±D	1D	—	—	—	—	—			
142	—	—	—	—	—	—	—			
149	—	—	—	—	—	—	—			
156	—	—	—	—	—	—	—			
164	—	—	—	—	—	—	—			
177	—	1D	—	—	—	—	—			
191	—	—	—	—	—	—	—			
205	—	—	—	—	—	—	—			
220	—	—	—	—	—	—	—			
233	—	—	—	—	—	—	—			
260	—	—	—	—	—	—	—			
318	—	1D	—	—	—	—	—			
348	±D	—	—	—	—	—	—			
450	—	—	—	—	—	—	—			
464	—	—	—	—	—	—	—			
529	—	—	—	—	—	—	—			
794	—	—	—	—	—	—	—			
812	—	—	—	—	—	—	—			
1,656	—	—	—	—	—	—	—			
2,051		—	—	—	—	—	—			
2,223	—	—	—	—	—	—	—			

P—Positive.
D—Doubtful.

of the Mazzini, had become negative, and no significant degree of positivity has since been recorded. There was a lapse from observation of 28 months; negative serologic findings were recorded prior to the lapse and again upon the resumption of observation. At the time of the last observation, 74 posttreatment months, the patient was clinically and serologically negative.

Chart 2 displays the diagnostic and follow-up data for the second patient treated. All of the serologic tests were negative by the fiftieth day. At the completion of 785 days of posttreatment observation, the patient was still clinically and serologically negative. Then there was a 41-month lapse from observation. Finally the patient was located and again brought under observation, 67 months after therapy. The clinical and serologic picture was negative before and after the lapse, and has remained so through the seventy-second month of observation.

Clinical and serologic information for the third patient is shown in chart 3.

Chart 2

Patient 2: E. D., Chinese, male, 24 years old.
History: No previous venereal disease. Incubation—48 days.
Chancre: Penile, darkfield-positive.
Diagnosis: Primary syphilis—10 days.
Treatment: 25,000 units of penicillin every 4 hours for 48 injections; date begun: June 28, 1943.
Reaction: Malaise, headache; temperature: 38.2° C. Enlarged, painful inguinal glands. 12 days—ulcer healed.

Period of observation (days)	Qualitative methods							Quantitative methods		
	Kline exclusion precipitation	Mazzini flocculation	Kline diagnostic precipitation	Kahn standard precipitation	Hinton flocculation	Eagle flocculation	Kolmer simplified complement-fixation	Mazzini flocculation	Kahn precipitation	
										Units
0	3	3	±D	3	P	P	4	2 1 — — —	4 2 — — —	8
1	4	4	±D	3	P	P	4	2 1 — — —	4 1 — — —	4
9		4		3	P	P	4	4 2 — — —	4 2 — — —	8
23	1D	2D	—	2	—	—	4	2 1 — — —	4 ± — — —	4
30	1D	1D	—	±D	—	—	1	1 — — —	2 — — — —	4
37	—	1D	—	—	—	—	±D	1 — — —	1 — — —	<1
44	—	—	—	—	—	—	4			
51	—	1D	—	—	—	—	—	1 — — —		
58	—	—	—	—	—	—	—			
65	—	—	—	—	—	—	—			
72	—	—	—	—	—	—	—			
79	—	—	—	—	—	—	—			
84	—	—	—	—	—	—	—			
94	—	—	—	—	—	—	—			
101	—	—	—	—	—	—	—			
107	—	—	—	—	—	—	—			
114	—	—	—	—	—	—	—			
121	—	—	—	—	—	—	—			
128	—	—	—	—	—	—	—			
135	—	—	—	—	—	—	—			
142	—	—	—	—	—	—	—			
156	—	—	—	—	—	—	—			
170	—	—	—	—	—	—	—			
194	—	—	—	—	—	—	—			
208	—	—	—	—	—	—	—			
258	—	—	—	—	—	—	—			
298	—	—	—	—	—	—	—			
412	—	1D	—	—	—	—	—			
427	—	—	—	—	—	—	—			
785	—	—	—	—	—	—	—			
2,034	—	—	—	—	—	—	—			
2,169		—		—	—	—	—			

P— Positive.
D—Doubtful.

Chart 3

Patient 3: H. J., white, male, 21 years old.
History: Chancroid 8 months previous; three negative blood tests since. Incubation—31 days.
Chancre: Penile, darkfield-positive.
Diagnosis: Primary syphilis—8 days.
Treatment: 25,000 units of penicillin every 4 hours for 85 injections; date begun: June 29, 1943.
Reaction: Malaise, headache; temperature 37.5° C. Acute edema of prepuce and pain at base of lesion.

Period of observation (days)	Qualitative methods							Quantitative methods		
	Kline exclusion precipitation	Mazzini flocculation	Kline diagnostic precipitation	Kahn standard precipitation	Hinton flocculation	Eagle flocculation	Kolmer simplified complement-fixation	Mazzini flocculation	Kahn precipitation	*Units*
0	4	4	2	4	P	P	4	4 3 2 1 — — — —	4 4 4 4 2 — — — —	64
1	3	4	2	4	P	P	4	4 4 2 1 1 — — —	4 4 4 4 2 — — — —	64
8		4		4	P	P	4	4 4 3 1 1 — — —	4 4 4 3 2 ± — — —	64
15		4		3	P	P	4	3 3 2 1 1 — — —	4 4 4 2 ± — — — —	32
22	3	3	1D	2	P	—	4	2 1 1 1 — — — —	4 3 1 1 — — — — —	8
29	1D	1D	—	2	D	—	4	1 1 1 — — — — —	2 ± ± — — — — — —	2
36	—	1D	—	—	—	—	2	1 1 1 — — — — —	± — — — — — — — —	—
43	—	—	—	—	—	—	4			
50	—	—	—	—	—	—	—			
57	—	1D	—	—	—	—	—			
64	—	—	—	—	—	—	—			
71	±D	1D	—	—	—	—	—			
78	—	—	—	—	—	—	—			
85	—	1D	—	—	—	—	—			
93	—	—	—	—	—	—	—			
100	—	—	—	—	—	—	—			
107	—	—	—	—	—	—	—			
223	—	—	—	—	—	—	—			
1,532	—	—	—	—	—	—	—			
1,989		—		—	—	—	—			
2,165		—		—	—	—	—			

P—Positive. D—Doubtful.

Following treatment, there was a rapid reversal of the serologic tests to the negative phase. The patient was clinically and serologically negative at the completion of 223 days of posttreatment observation. A 43-month lapse from observation occurred, during which it is believed the serologic reaction remained negative, since it was negative both preceding and following the lapse. The patient was clinically and serologically negative at the end of 72 months of posttreatment observation.

In chart 4, the record of the fourth patient presents one of the interesting aspects of rapid syphilotherapy—reinfection. All serologic tests were recorded as negative on the seventy-first posttreatment day, but a return to the positive reactions was noted on the two hundred and eighty-sixth day. A darkfield-positive lesion had developed on the lower lip. The patient was re-treated with a more intensive penicillin schedule. During the course of therapy, the serologic titer reached a high level and then declined. The serologic curve remained in the doubtful zone for some time but did not return to a high-titer level. All tests were recorded as negative on the nine hundred and ninety-second day and remained so up to the last observation, 72 months after the initial therapy.

Chart 4

Patient 4: S. I., Negro, male, 18 years old.
History: 8 gonorrheal infections between 1936 and 1943. Incubation—39 days.
Chancre: Penile, darkfield-positive.
Diagnosis: Primary syphilis—8 days.
Treatment: 25,000 units penicillin every 4 hours for 48 injections; date begun: July 6, 1943.
Reaction: Mild systemic Herxheimer 6 hours after start of treatment. 10 days—ulcer healed.
Basis for re-treatment:

1. Development of gonorrheal urethritis, 273 posttreatment days; treated with penicillin.
2. Development of darkfield-positive lesion on lower lip, 303 posttreatment days; ulcer healed on 309th day.

Re-treatment: 40,000 units penicillin every 3 hours for 60 injections—318 days after original therapy.
Remarks: 13 gonorrheal infections between 9th posttreatment day and 52nd posttreatment month.

Period of observation (days)	Qualitative methods							Quantitative methods		
	Kline exclusion precipitation	Mazzini flocculation	Kline diagnostic precipitation	Kahn standard precipitation	Hinton flocculation	Eagle flocculation	Kolmer simplified complement-fixation	Mazzini flocculation	Kahn precipitation	*Units*
0		1D		—	—	—	—	— — — — — —	— — — — — —	—
1	4	4	±D	1D	—	P	—	2 1 — — — —	3 ± — — — —	1
8		4		3	—	P	4	3 2 — — — —	4 4 ± — — —	8
15	4	4	1D	3	P	P	±D	4 3 2 1 — —	4 3 1 — — —	8
22	4	3	±D	3	P	D	±D	3 1 — — — —	4 1 ± — — —	4
30	1D	2D	±D	—	D	—	±D	2 1 — — — —	1 — — — — —	< 1
36	±D	2D	—	—	—	—	—	2 — — — — —	± — — — — —	—
43	—	2D	—	—	—	—	—	2 1 — — — —	± — — — — —	—
50	±D	1D	—	—	—	—	—	1 — — — — —	— — — — — —	—
57	—	1D	—	—	—	—	—	1 — — — — —	± — — — — —	—
64	±D	1D	—	—	—	—	—	1 — — — — —	— — — — — —	—
71	—	—	—	—	—	—	—			
86	—	—	—	—	—	—	—			
93	—	—	—	—	—	—	—			
99	—	—	—	—	—	—	—			
106	—	—	—	—	—	—	—			
115		—		—	—	—	—			
120	—	—	—	—	—	—	—			
156	—	—	—	—	—	—	—			
168	—	—	—	—	—	—	—			
181	±D	—	—	—	—	—	—			
199	—	—	—	—	—	—	—			
220	—	1D	—	—	—	—	—			
265	—	—	—	—	—	—	—			
286	4	4	2	4			4			
295	4	4	4	4		P	4	4 4 4 2 1 — — — — —	4 4 1 ± — — — — — —	8
318	4	4	4	4	P	P	4	4 4 4 4 4 3 1 — — —	4 4 4 4 4 3 — — — —	128
326	4	4	4	4	P	P	4	4 4 4 4 4 4 3 1 — —	4 4 4 4 4 4 1 — — —	128
337	4	4	4	4	P	P	4	4 4 4 4 4 3 — — — —	4 4 4 4 4 2 — — — —	128
344	4	4	4	4	P	P	4	4 4 4 4 3 1 — — — —	2 4 4 4 4 ± — — — —	64
357	4	4	4	4	P	P	4	4 4 4 4 2 — — — — —	4 4 4 4 ± — — — — —	32
422	2	3	±D	1D	P	P	±D			1
433	1D	3	—	1D	D	P	4			1
442	1D	3	±D	1D	—	P	3			1
455	2	2D	±D	2	D	P	4			2
482	1D	1D	±D	1D	D	P	—			1
489	±D	2D	—	2	D	P	±D			2
496	2	2D	±D	1D	—	P	1			1

Chart 4—Continued

Period of observation (days)	Qualitative methods							Quantitative methods		
	Kline exclusion precipitation	Mazzini flocculation	Kline diagnostic precipitation	Kahn standard precipitation	Hinton flocculation	Eagle flocculation	Kolmer simplified complement-fixation	Mazzini flocculation	Kahn precipitation	
										Units
566--	±D	2D	—	—	—	D	—			—
588--	±D	1D	—	—	D	D	—			—
595--	±D	1D	—	—	D	D	—			—
664--	±D	4	—	±N	—	—	—	4 4 3 1 — — —		—
715--	—	1D	—	—	—	—	—			—
769--	±D	1D	—	—	—	—	±D			
822--	±D	1D	—	—	D	D	—			
844--	±D	1D	—	—	—	—	—			
854--	±D	1D	—	—	—	—	—			
892--	—	1D	—	—	—	—	—			
929--	—	1D	—	—	—	—	±D			
992--	±D	—	—	—	—	—	—			
1121	—	—	—	—	—	—	—			
1266	—	—	—	—	—	—	—			
1553	—	—	—	—	—	—	—			
1902		—		—	—	—	—			
2164		—		—	—	—	—			

P—Positive.
D—Doubtful.

In the preliminary report, reference was made to the apparent haste displayed in employing the antibiotic in human disease prior to its complete assay in the animal. This deviation from the procedure usually employed in the development of a new therapy appears to have been vindicated. More frequent conduct of pilot studies in the human being deserves serious consideration in instances in which the product under scrutiny is known to be nontoxic and in which its trial would not jeopardize the chance of securing relief through conventional forms of treatment should the experimental therapy fail.

It was also intimated in the preliminary report that, if the findings of the pilot study were substantiated by a more thorough study, the entire structure of syphilotherapy might undergo complete realignment. Surely this has been taking place in the last several years. It is hoped that the simpler methods of treatment may soon become part of the syphilis control mechanism of this country and that they will, thereby, exert a favorable influence upon the future prevalence of the infection.

In the original report, mention was also made of the need for coordinated studies designed to portray the optimal time-dose relationship for the new agent. Much has been done in this direction through the broad-scale effort of the National Research Council and, more recently, by the National Institutes of Health. Each improvement in the product itself has made less useful the findings obtained with the earlier preparations and has necessitated the repetition of studies both in the animal and in man.

The effectiveness of penicillin in the treatment of early syphilis has been confirmed by 6 years of posttreatment observation of the four patients who were the subject of the preliminary report on the penicillin treatment of early syphilis.

Reference

1. Mahoney, J. F.; Arnold, R. C.; Harris, A.: Penicillin treatment of early syphilis. A preliminary report. Ven. Dis. Inform., 24: 355–357, December 1943.

CURRENT NOTES AND REPORTS

Social Hygiene Day, 1950

February 1, 1950, marks the local community observances of Social Hygiene Day, with the largest meeting scheduled for New York City at the Hotel New Yorker.

These observances are designed to enlist citizen support of social hygiene objectives, which this year stress education to prevent venereal infections, particularly through training of youth through home, church, and school for successful marriage and family life. The slogan for Social Hygiene Day, 1950, is "Social Hygiene is a Family Affair."

Held under the national sponsorship of the American Social Hygiene Association, with the cooperation of the United States Public Health Service, the observances in thousands of cities and towns in the United States and the Territories serve to focus public attention on the need for social hygiene programs and to spark year-round efforts.

All avenues of reaching the public, including newspapers, magazines, radio, and television serve to channel out publicity on the events of the Day, which in many areas are officially proclaimed by governors of States and mayors of cities. To aid in planning these local events, the Association is preparing an attractive illustrated publication for wide distribution, along with informational materials.

Any communities which have not yet instituted annual observance but which wish to participate in or to launch a social hygiene society, may get suggestions and free materials by writing to the Social Hygiene Day Service, American Social Hygiene Association, 1790 Broadway, New York 19, N. Y.

New York Venereal Disease Seminars

A series of lectures and demonstrations, for all interested physicians, on the diagnosis, treatment, and management of venereal diseases started at the New York City Department of Health on Saturday morning, October 8. There are to be 12 weekly meetings presided over by experts in the various special fields of venereal disease control. Sessions are starting at 10:30 a. m. in the second floor auditorium of the health department, 125 Worth Street, New York City. Another series of lectures is planned for 1950. The schedule of lectures includes:

October 8:	The Medical Practitioner and Venereal Disease. Dr. Walter P. Anderton, Associate Professor, Clinical Medicine, College of Physicians and Surgeons.
October 15:	Current Developments in the Treatment of Syphilis. R. C. Arnold, Director, Venereal Disease Research Laboratory, United States Public Health Service.

October 22:	Surgeon, Harlem Hospital. Aureomycin in Venereal Disease. Dr. Aaron Prigot, Associate
October 29:	Primary Syphilis–Differentiation from Other Genital Lesions. Dr. Frank C. Combes, Professor, Dermatology and Syphilology, New York University-Bellevue Medical School.
November 5:	Skin Lesions of Syphilis and Their Differential Diagnosis. Dr. Royal M. Montgomery, Adjunct Professor, Dermatology and Syphilology, New York Polyclinic Hospital.
November 12:	Chancroid, Lymphogranuloma Venereum, and Granuloma Inguinale. Dr. Borris Kornblith, Associate Surgeon, Gouverneur Hospital.
November 19:	Heart Disease and Syphilis in the General Practitioner's Office. Dr. Edwin P. Maynard, Professor, Clinical Medicine, Long Island Medical College.
November 26:	Syphilis of the Central Nervous System. Dr. Bernhard Dattner, Associate Neuropsychiatrist, Bellevue Hospital.
December 2:	*Special Meeting, Friday, 1:30–2:30 p. m.* The Oral Manifestations of Syphilis and Their Differential Diagnosis, of Interest to Medical and Dental Practitioners. J. W. Richter, D.D.S.
December 3:	Serodiagnosis of Syphilis. Dr. Charles R. Rein, Serologist, Skin and Cancer Unit of the Post Graduate Medical School, New York University–Bellevue Medical Center.
December 10:	The Public Health Nurses' Role in the General Practitioner's Approach to Venereal Disease. Miss Hortense Hilbert, R. N.
December 17:	The Syphilitic Pregnant Woman and Her Expected Child. Dr. Mortimer B. Speiser, Assistant Professor, Obstetrics and Gynecology, New York University Medical School.

District of Columbia Stars VD Patients in Documentary Radio Spots

Documentary radio with a different twist is a feature of the VD campaign started October 1 by the District of Columbia Health Department. To be aired by local stations, spot announcements with the voices of syphilitic patients describing their own cases have been recorded. An introduction is given by Gunnar Back, a former CBS commentator and an old hand at VD radio, and a closing statement is made giving the phone number to be called for further details.

Plans for the present campaign were built on the success of a radio program series produced by the Department and broadcast by 3 D. C. area radio stations last spring. The 13-program series was credited with bringing many patients in for treatment. Aimed specifically at women, each program told the real life stories of infected patients through the combined technics of narration and patient interview. Patients found to fit the individual program subject were interviewed by a prominent local actress, who also did the narration.

A survey taken following this radio series and the accompanying press campaign pointed up the need for a committee composed of representatives from prominent community groups. Sixty-five organizations were approached with all but two offering their cooperation in a city-wide mobilization against venereal disease.

Campaign organizers said the present drive was the first of its kind to be undertaken in the District of Columbia, in that every type of civic organization has been called upon to take part, including business, professional, veterans', and church groups. A year's program with intensive effort during the first 2 months is planned. The drive started with a local television show introducing the purpose of the campaign—to step up volunteer reporting for treatment of VD patients. The aim of the committee is to make the VD program a community project and not simply a health department effort.

Paul Whiteman Airs VD Records

Three of the new VD records have been featured in a coast-to-coast airshow on the ABC network. "Put Old VD Down," "I've Got Good News," and "That Ignorant, Ignorant Cowboy" were played by Paul Whiteman on his "disc jockey" program at 10 p. m. e. s. t., September 27. During the program, the pamphlet "We're Healthy—Are You?" was offered to those who wished to write in. Letters were received from 164 communities spread throughout 42 States and the District of Columbia.

The first of the records, "Put Old VD Down," was produced by the District of Columbia Health Department and has been a key performer in the District's recent venereal disease campaign.

"I've Got Good News" is a product of the Communication Materials Center, Columbia University Press, as is "That Ignorant, Ignorant Cowboy." The latter disc will be heard in juke boxes across the country under an agreement between a record company and a cooperative organization of juke-box operators. The company and the operators are teaming up to put 250,000 copies of the record in juke joints over the United States, as a public service.

"Diagnosis of Syphilis" Published

A revision of "The Diagnosis of Syphilis by the General Practitioner," by Dr. Joseph Earle Moore, Special Consultant to Public Health Service, has been published as Supplement 23 to The Journal of Venereal Disease Information. This is the 1949 version of Supplement 5, issued in 1938 and 1940.

The major change embodied in this latest supplement is the addition of a completely new section on the interpretation of laboratory tests for syphilis. It offers a discussion of the various technics used in blood and spinal fluid tests, affording the general practitioner a comprehensive source of information as to the selection of a good laboratory and the interpretation of the results provided by it.

In the first part of the supplement, the clinical diagnosis of syphilis is covered in detail. Both the text and the outline charts of "suspicion arousers" are already familiar to users of the earlier editions. Dr. Moore repeatedly underlines his advice to "do a blood serologic test." He reasserts the important role that the doctor still has to play if syphilis is eventually to be brought under control.

Supplement 23 can be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., for 25 cents per copy. A discount of 25 percent is allowed on orders of 100 or more sent to a single address.

CURRENT LITERATURE

NOTE: Abstracts of all articles listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 20 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

AM. J. DIS. CHILD., CHICAGO

*Treatment of infantile congenital syphilis. Results with aqueous penicillin alone in sixty infants followed for an average of two years after treatment. Elizabeth Kirk Rose, Paul György and Norman R. Ingraham, Jr., 77: 729–735, June 1949.

Treatment of infantile congenital syphilis. Results with aqueous penicillin alone in sixty infants followed for an average of two years after treatment. Elizabeth Kirk Rose, Paul György and Norman R. Ingraham, Jr. Am. J. Dis. Child., 77: 729–735, June 1949.

The results of long-term follow-up observation in 60 infants with congenital syphilis who were treated with penicillin are reported.

Fifty-five patients received aqueous penicillin administered intramuscularly in doses varying from 20,000 to 200,000 units per pound (44,000 to 440,000 per kilogram) of body weight.

Five infants were treated with penicillin by mouth. A buffered preparation of calcium penicillin was used in dosages varying from 1,500,000 to 2,500,000 units. Tablets of 12,500 units were given every 3 hours.

There were seven deaths in the group of infants receiving intramuscular penicillin, none of which could be considered due to penicillin therapy.

Follow-up studies included regular visits, at which time were noted serologic titers, physical examination and roentgenologic examination of the bones when previous abnormalities existed. Yearly examination of cerebrospinal fluid was planned. The average length of the period of observation was 2 years on 52 of the 53 surviving patients—only 1 patient having been lost to follow-up study. The shortest follow-up periods were 59, 85, 92, and 106 days, and the longest, 1,339, 1,343, 1,362, and 1,432 days.

Of the 48 living patients treated with penicillin intramuscularly, 37 were apparently cured (clinically well and with seronegative reactions); 7 were clinically well but still showed seropositive reactions, though the titer was declining; 3 were clinically well but revealed no change in titer. Two of the latter were recently re-treated.

Of the five patients treated with penicillin by mouth, four infants responded satisfactorily. One older child 2⅓ years of age responded well, but his reaction remained seropositive after re-treatment.

The age of the patient at the onset of treatment, rather than the dosage, type or means of administration of penicillin, seemed to be the chief factor in determining satisfactory response. Cures approached 100 percent when treatment was commenced before the third month of life.

AM. J. SYPH., GONOR. & VEN. DIS., ST. LOUIS

*The duration of acquired immunity in experimental syphilis. Harold J. Magnuson, Barbara J. Rosenau and J. W. Clark, Jr. 33: 297–302, July 1949.

*Studies of the life and motility of *Treponema pallidum* in fertile hens' eggs. Richard J. Rowe and Arthur C. Curtis. 33: 303–307, July 1949.

The duration of acquired immunity in experimental syphilis. Harold J. Magnuson, Barbara J. Rosenau and J. W. Clark, Jr. Am. J. Syph., Gonor. & Ven. Dis., 33: 297–302, July 1949.

The purpose of this article, a continuation of earlier studies, is to describe the degree of established immunity as measured by challenge at varying time intervals after termination of the original 12-week immunizing infection.

Male rabbits were inoculated in a single testis with 10^6 *Treponema pallidum* (Nichols strain). The original infection was confirmed by darkfield examination of tissue obtained by testis puncture. Twelve weeks after inoculation, the infection was terminated by the administration of four daily doses of penicillin G in peanut oil-beeswax. The challenging inoculation was made 6, 12, 24, or 48 weeks after treatment. The suitably calibrated challenge inoculation was made into the originally inoculated testis, and the size of challenging inoculums varied between 2×10^2 to 10^7 organisms. Animals were examined twice weekly following reinoculation to detect development of any local lesions. The development of a darkfield-positive syphiloma at the site of inoculation was considered symptomatic reinfection. If no symptomatic lesions were observed during the 3-month period following inoculation, the animals were sacrificed, both popliteal nodes removed, emulsified, and inoculated into the testes of two node transfer animals in the usual manner. The node transfer animals were examined semiweekly for a 3-month period, and material from any suspicious testicular lesions was examined by darkfield. If the node transfer animals were positive, the parent animal was considered to have developed an asymptomatic reinfection. The node transfer animals were considered negative only if they remained negative throughout the 3-month observation. If the original parent was clinically negative and if the node transfer animals were negative, the parent animal was considered immune to the inoculum employed.

Since none of the animals developed symptomatic reinfection, the symptomatic 50-percent infectious dose was greater than the largest challenge employed. No symptomatic reinfections were obtained with inoculums as large as 2×10^5 organisms. The asymptomatic 50-percent infectious inoculum was approximately 5×10^3 organisms. The present results would indicate that once immunity has been developed it persists for a considerable period of time. Such immunity would, therefore, appear to be rather permanent. None of the animals, whether asymptomatically reinfected or whether immune, showed any significant rise in serologic titer following reinoculation.

Studies of the life and motility of *Treponema pallidum* in fertile hen's eggs. Richard J. Rowe and Arthur C. Curtis. Am. J. Syph., Gonor. & Ven. Dis., 33: 303–307, July 1949.

The authors attempted to graft *Treponema pallidum* infected tissue onto the chorioallantoic membranes of hens' eggs and to determine whether in these preparations infectivity could be correlated with the presence of spirochetes.

Fertile hens' eggs were incubated for periods of 6 to 11 days prior to inoculation. Infected testicles were removed at 29 to 89 days after inoculation with a darkfield-positive source of the Nichols strain of *T. pallidum*. Darkfields were done on testicular material before implantation and on the grafts of each egg at the end of the period of observation. Infected tissue was placed on the chorioallantoic membranes in 11 different instances, 9 to 14 eggs being used each time.

In one experiment, tissue was allowed to remain on the membranes for a period of 14 days at 35° C. Ten nonmotile spirochetes were found in one egg and five in another. None were found in the remaining six. The tissue from these eight eggs was pooled and inoculated intratesticularly into a rabbit. At the end of 121 days there was no palpable nodule present in the testicle. At the end of 125 days, both standard and quantitative Kahn serologic tests were negative.

In the other experiments, spirochetes

were found in eight eggs at the end of 7 days. In two experiments in which eggs were incubated at 33° C., active spirochetes with morphology and motion typical of *T. pallidum* were present. Tissues from these were inoculated into the testicles of two adult rabbits. One rabbit developed a darkfield-positive syphiloma in 23 days and the other in 32 days.

Of a total of nine rabbits inoculated, one died and six developed darkfield-positive syphilomas. The spirochetes from these syphilomas had motion and morphology typical of *T. pallidum.*

The authors feel that they have not demonstrated growth of *T. pallidum* in fertile hens' eggs. Use of younger spirochetes, use of human tissue, and incubation of the eggs at 33° C. may give better results.

BULL. ACAD. MED. CLEVELAND, CLEVELAND

Syphilis and pre-marital law. G. A. DeOreo. 34 : 9, 25, Feb. 1949.

CANAD. J. PUB. HEALTH, TORONTO

Premarital health examinations in Saskatchewan : problems and results. H. S. Doyle. 40 : 200–207, May 1949.

CANAD. M. A. J., MONTREAL

Penicillin treatment in early syphilis. Walter J. Cole and L. D. Proctor. 60 : 480–483, May 1949.

CHRON. WORLD HEALTH ORGAN., GENEVA

Venereal disease in Germany. 3 : 111–114, May 1949.

ILLINOIS HEALTH MESSENGER, SPRINGFIELD

Public health detectives. 21 : 33–34, May 1, 1949.

ILLINOIS M. J., OAK PARK

Report of the committee on venereal disease control. 96 : 70–73, July 1949.

INDIAN J. VEN. DIS., BOMBAY

A scheme for the control and prevention of venereal diseases. V. Govindan Nair. 15 : 35–44, Apr.–June 1949.

Influence of vitamin C in syphilitic rashes. K. D. Lahiri. 15 : 45–46, Apr.–June 1949.

Venereal diseases and long-acting penicillins. A. R. Raychaudhury. 15 : 46–50, Apr.–June 1949.

J. PHILIPPINE M. A., MANILA

Resolution of the committee for the control of venereal diseases of the national advisory health council against the proposed establishment of red-light district in the Philippines. News Items. 24 : 106–107, Feb. 1948.

The diagnosis and treatment of venereal diseases. Jose Amador Guevera, T. Yusay, J. O. Quiazon, F. Hipolito, A. Zalamea and S. Montenegro. Abstracts of Lectures Given During the Brief Post Graduate Course in Venereology, Feb. 22–Mar. 4, 1949, Manila. 25 : 148, Mar. 1949.

J. UROL., BALTIMORE

Cystitis : classification and treatment ; discussion of type occurring after transurethral resection. [V.D.] Charles Pierre Mathé. 62 : 308–316, Sept. 1949.

Erratum

On page 303 of the October issue, the first reference under *M. Ann. District of Columbia* should read as follows :

The clinical use of aureomycin. Emanuel B. Schoenbach. 18 : 290–293, 333, June 1949.

STATISTICS

Contact Investigation Indices, January 1944–December 1948, Based on Previously Untreated Primary and Secondary Syphilis Admissions

Area	Clinic and rapid treatment center admissions (previously untreated)										Contacts obtained per admission									
	1944		1945		1946		1947		1948		1944		1945		1946		1947		1948	
	[1] 1	[2] 2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
Alabama				325	1,260	1,210	1,919	1,769	1,374	987				0.43	1.39	2.41	2.43	3.56	3.97	4.73
Arkansas				488	792	779	863		690	397				2.03	1.45	1.21	1.86		2.79	2.46
California										703										1.88
Colorado					192	161	191	99	94	74					1.43	1.94	1.40	3.03	2.02	3.41
District of Columbia	366	384	359	339	458	512	546	648	429	422	1.29	1.16	1.92	1.67	2.02	2.04	1.70	1.67	2.13	2.73
Florida	324	435	919	825	1,213	1,563	1,320	1,180	1,837	1,036	.95	1.32	1.36	2.05	1.47	.84	1.16	1.21	1.68	1.73
Georgia			942	905	1,611	1,355		1,698	1,430	1,289			.63	3.38	1.28	1.67		2.69	3.40	3.24
Idaho									61	27									1.74	3.11
Indiana										394										1.87
Iowa						106	97		136	63						.99	1.73		1.35	1.41
Kansas			65	67	61	51	137	172	74	83			1.12	1.42	3.95	3.31	1.49	.61	.62	.51
Kentucky		546	630	935	1,271	1,212	1,052	872	671	474		1.09	1.69	1.97	1.79	1.69	1.38	1.34	1.60	1.60
Louisiana					1,948		1,439	1,491							1.86		2.31	1.76		
Maine									76	30									.70	.53
Michigan				835	795	721	616	631	504	544				.98	1.51	1.58	1.60	1.26	1.72	2.05
Mississippi			1,361	1,280	1,963	1,946	2,350	1,526	1,290	1,063			1.77	2.26	2.14	2.47	2.38	3.06	3.60	3.43
Nebraska					116	87	102	51	47	45					.88	1.32	1.46	2.25	2.02	1.93
New Mexico								102	79	80								1.61	1.46	1.74
North Carolina		1,104	1,148	1,121	1,868	1,956	2,020	1,649	1,506	1,225		1.56	2.70	2.68	2.37	2.01	1.90	2.18	2.22	2.20
Ohio					1,160	1,657									.68	.87				
Oklahoma	256	204	270	363	543	515		377	438	401	1.77	1.62	1.79	2.12	2.38	1.63		2.05	1.80	2.25
Oregon										80										1.53
South Carolina	435	332	487	531	763	705	1,027	1,046	882	787	1.17	1.70	2.58	4.97	3.04	1.69	3.34	3.57	4.04	4.78
Texas					3,108	2,593	1,699	1,485	1.671	1,444					1.04	1.38	2.32	2.20	2.36	2.20
Virginia							984	899	718	469							1.06	1.80	1.92	2.14
West Virginia			606	654	1,108	1,227	639	597	367	297			1.24	1.82	1.52	1.92	2.54	2.02	3.24	2.47
Wisconsin							58	43	31	62							1.24	.51	.71	1.06
Chicago			709	1,106	1,333	1,032	1,029	851	651	569			1.38	1.62	1.98	1.58	1.48	.90	.99	1.45
New York City		1,767	611	673	1,284	1,369	1,003	775	592	526		1.23	1.43	1.19	1.54	.87	1.23	1.16	1.10	1.05
St. Louis	212	271	336	534	539	663	597		216	206	1.47	2.07	2.82	1.94	2.46	2.02	2.42		1.43	1.12
Seattle										55										2.00
Total	1,593	5,043	8,443	10,981	23,386	21,420	19,688	17,961	15,864	13,832	1.25	1.38	1.71	2.13	1.68	1.62	1.98	2.18	2.49	2.55
Total for 15 areas					16,793	16,345	15,650	13,351	11.989	9,576					1.70	1.70	2.00	2.20	2.48	2.64

Area	Contacts infected with syphilis per admission (Epidemiologic Index)										Contacts brought to treatment with syphilis per admission										Contacts brought to treatment with syphilis lesions per admission									
	1944		1945		1946		1947		1948		1944		1945		1946		1947		1948		1944		1945		1946		1947		1948	
	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
Alabama	----	----	----	0.10	0.36	0.59	0.68	1.11	1.27	1.40	----	----	----	0.07	0.19	0.30	0.40	0.66	0.73	0.84	----	----	----	0.04	0.05	0.08	0.10	0.12	0.13	0.12
Arkansas	----	----	----	.67	.39	.39	.77	----	.77	.67	----	----	----	.31	.27	.23	.38	----	.37	.36	----	----	----	.11	.13	.12	.19	----	.13	.12
California	----	----	----	----	----	----	----	----	----	.38	----	----	----	----	----	----	----	----	----	.20	----	----	----	----	----	----	----	----	----	.12
Colorado	----	----	----	----	.44	.50	.34	.61	.57	.70	----	----	----	----	.21	.27	.23	.35	.39	.45	----	----	----	----	.16	.19	.13	.12	.23	.31
District of Columbia	0.42	0.32	0.54	.43	.51	.44	.39	.51	.72	.74	0.16	0.11	0.26	.22	.30	.21	.19	.27	.34	.31	0.06	0.04	0.12	.09	.15	.11	.09	.12	.16	.18
Florida	.26	.38	.37	.55	.37	.36	.35	.37	.44	.51	.12	.14	.12	.30	.24	.31	.25	.17	.25	.33	.04	.07	.05	.17	.15	.22	.14	.10	.16	.15
Georgia	----	----	.25	.96	.43	.55	----	.83	1.07	.99	----	----	.10	.43	.19	.22	----	.32	.48	.54	----	----	.05	.15	.07	.11	----	.12	.20	.23
Idaho	----	----	----	----	----	----	----	----	.82	.44	----	----	----	----	----	----	----	----	.44	.19	----	----	----	----	----	----	----	----	.43	.19
Indiana	----	----	----	----	----	----	----	----	----	.49	----	----	----	----	----	----	----	----	----	.33	----	----	----	----	----	----	----	----	----	.24
Iowa	----	----	----	----	----	.25	.41	----	.29	.33	----	----	----	----	----	.12	.16	----	.14	.22	----	----	----	----	----	.08	.12	----	.07	.16
Kansas	----	----	.22	.28	1.00	.84	.36	.19	.18	.27	----	----	.12	.18	.70	.57	.23	.13	.15	.19	----	----	.09	.13	.47	.39	.20	.12	.15	.14
Kentucky	----	.30	.52	.54	.52	.56	.57	.51	.59	.57	----	.22	.38	.39	.29	.24	.22	.22	.23	.21	----	.15	.24	.27	.17	.14	.15	.13	.13	.14
Louisiana	----	----	----	----	.57	----	.90	.62	----	----	----	----	----	----	.35	----	.53	.35	----	----	----	----	----	----	.09	----	.26	.18	----	----
Maine	----	----	----	----	----	----	----	----	.42	.13	----	----	----	----	----	----	----	----	.24	.10	----	----	----	----	----	----	----	----	.22	.10
Michigan	----	----	----	.27	.48	.45	.60	.42	.53	.64	----	----	----	.16	.25	.19	.23	.16	.22	.29	----	----	----	.07	.10	.09	.10	.06	.11	.14
Mississippi	----	----	.52	.69	.63	.70	.62	.81	1.03	.88	----	----	.31	.41	.35	.45	.42	.51	.60	.46	----	----	.14	.16	.16	.23	.21	.27	.30	.21
Nebraska	----	----	----	----	.26	.47	.57	.96	.74	.58	----	----	----	----	.14	.38	.25	.57	.32	.29	----	----	----	----	.09	.28	.14	.29	.15	.16
New Mexico	----	----	----	----	----	----	----	.25	.20	.36	----	----	----	----	----	----	----	.16	.16	.28	----	----	----	----	----	----	----	.09	.15	.08
North Carolina	----	.52	.80	.77	.74	.67	.67	.62	.70	.63	----	.23	.28	.29	.31	.28	.37	.32	.35	.32	----	.12	.12	.16	.19	.18	.16	.19	.20	.19
Ohio	----	----	----	----	.15	.22	----	----	----	----	----	----	----	----	.08	.11	----	----	----	----	----	----	----	----	.03	.06	----	----	----	----
Oklahoma	.46	.50	.51	.67	.82	.57	----	.70	.72	.73	.24	.22	.27	.33	.40	.30	----	.39	.38	.39	.09	.14	.12	.17	.18	.17	----	.23	.26	.26
Oregon	----	----	----	----	----	----	----	----	----	.60	----	----	----	----	----	----	----	----	----	.45	----	----	----	----	----	----	----	----	----	.34
South Carolina	.42	.55	.84	1.19	.66	.40	.68	.66	.90	1.13	.17	.18	.36	.45	.28	.29	.40	.34	.53	.63	.05	.07	.11	.17	.10	.13	.15	.11	.19	.20
Texas	----	----	----	----	.34	.42	.78	.76	.91	.70	----	----	----	----	.23	.26	.54	.49	.55	.45	----	----	----	----	.12	.13	.32	.27	.26	.26
Virginia	----	----	----	----	----	----	.30	.68	.70	.68	----	----	----	----	----	----	.15	.34	.34	.35	----	----	----	----	----	----	.07	.20	.20	.20
West Virginia	----	----	.40	.44	.45	.56	.88	.56	.86	.57	----	----	.20	.18	.19	.22	.30	.21	.31	.33	----	----	.12	.13	.13	.14	.17	.14	.18	.21
Wisconsin	----	----	----	----	----	----	.41	.21	.48	.39	----	----	----	----	----	----	.31	.16	.32	.34	----	----	----	----	----	----	.28	.12	.23	.18
Chicago	----	----	.32	.36	.53	.49	.60	.38	.58	.43	----	----	.16	.18	.27	.24	.35	.22	.33	.34	----	----	.08	.13	.16	.15	.22	.14	.20	.19
New York City	----	.26	.34	.23	.32	.29	.49	.31	.41	.43	----	.10	.17	.10	.17	.14	.20	.16	.18	.21	----	.04	.08	.05	.07	.06	.10	.07	.09	.13
St. Louis	.31	.39	.39	.34	.45	.24	.20	----	.24	.29	.21	.21	.22	.17	.29	.11	.10	----	.14	.18	.09	.09	.08	.05	.10	.03	.04	----	.05	.09
Seattle	----	----	----	----	----	----	----	----	----	.18	----	----	----	----	----	----	----	----	----	.15	----	----	----	----	----	----	----	----	----	.09
Total	.38	.37	.47	.58	.47	.48	.61	.66	.78	.72	.18	.16	.23	.29	.26	.25	.35	.35	.41	.41	.06	.08	.11	.14	.12	.13	.17	.16	.19	.19
Total for 15 areas	----	----	----	----	.48	.51	.62	.64	.77	.75	----	----	----	----	.26	.28	.35	.35	.42	.42	----	----	----	----	.13	.15	.17	.16	.19	.19

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[1] First half of calendar year. [2] Last half of calendar year.

Source: Special Semi-annual Contact Investigation Report tabulations, FSA-PHS—Division of Venereal Disease, Office of Statistics, 10/12/49 (DBB-NF).

AUTHOR INDEX

A

Page

Abraham, Sidney: Factors affecting the results of interviewing for contacts (OA) (Dec.) 341
Aiken, R. B.: Out-patient attendance of early syphilis patients treated by private physicians in Vermont (OA) (Apr.) 107
Altemeier, William A.: Results of systemic administration of the antibiotic, bacitracin, in surgical infections, preliminary report (AB) (July) 204
Altshuler, L.: Efficacy of penicillin treatment of early syphilis in the Army (AB) (Oct.) 299
Arnold, R. C.:
  Penicillin therapy of early syphilis: IV (OA) (May) 125
  Penicillin treatment of early syphilis—first four patients after six years (OA) (Dec.) 350
  Preservation and inoculation studies on *Treponema pallidum* (OA) (Apr.) 104
  Role of cardiolipin antigens in serology of syphilis (OA) (Aug.) 217

B

Babione, Robert W.: Ratio of gonorrhea to syphilis as occurring in the United States Navy (AB) (Nov.) 333
Baker, Amelia H.:
  Asexual syphilis in children (OA) (Jan.) 7
  Penicillin in abortive treatment of syphilis (OA) (Sept.) 252
Barnett, Charles W.: Prognosis in late latent syphilis (AB) (Sept.) 265
Barton, Robert L.: Granuloma inguinale. Review of literature and a report of 97 cases, with a note on streptomycin therapy (AB) (July) 205
Bauer, Theodore J.:
  Fever-chemotherapy in early syphilis (OA) (Mar.) 69
  Granuloma inguinale. Review of literature and a report of 97 cases, with a note on streptomycin therapy (AB) (July) 205
  Results of therapy by race, sex, and stage of syphilis (OA) (Jan.) 1
Benton, Curtis D., Jr.: Treatment of ocular syphilis with penicillin (AB) (Sept.) 266

Page

Blum, Henrik L.: Prognosis in late latent syphilis (AB) (Sept.) 265
Boak, Ruth A.: Therapeutic efficacy of penicillin G in experimental syphilis produced by five different strains of *Treponema pallidum* (AB) (July) 202
Boggs, Hunter: Report of spinal fluid findings in patients who "relapsed" following penicillin therapy for early syphilis (OA) (Aug.) 219
Bogue, Robert S.: Mass public venereal disease education—Ohio fairs (OA) (July) 196
Boone, Howard: Venereal disease case finding in Quitman County, Mississippi (OA) (May) 127
Bossak, Hilfred N.: Quantitative turbidimetric method for the determination of spinal fluid protein (OA) (Apr.) 100
Bowdoin, C. D.: Socioeconomic factors in syphilis prevalence, Savannah, Georgia (OA) (May) 131
Bowen, Jack H.: Quantitative serologic titer in post-treatment observation of early syphilis treated with penicillin (AB) (Nov.) 335
Bowman, Richard W.: Comparative studies on mailed spinal fluid specimens (OA) (Jan.) 11
Bucca, Matthew A.:
  Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301
Buck, T. C.:
  Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301
Bundesen, Herman N.: Penicillin in the treatment of early syphilis: 639 patients treated with 2,400,000 units of sodium penicillin in 7½ days (OA) (Nov.) 321

C

Cannefax, George R.:
  Comparative studies on mailed spinal fluid specimens (OA) (Jan.) 11
  Stable control serum for standardizing the sensitivity of tests used in diagnosis and control of syphilis (OA) (June) 169
Carpenter, Charles M.:
  Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301
  Therapeutic efficacy of penicillin G in experimental syphilis produced by five different strains of *Treponema pallidum* (AB) (July) 202

NOTE: OA, original article; AB, abstract; NR, Current Notes and Reports.

Page

Casman, E. P.:
  Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301
Cenac, Mark T.: Characteristics of the cerebrospinal fluid in lymphogranuloma venereum (OA) (Oct.) 291
Chen, Calvin H.:
  Experimental studies on the pathogenicity of *Donovania granulomatis* (AB) (Oct.) 300
  Oral aureomycin in therapy of streptomycin-resistant granuloma inguinale (AB) (Aug.) 237
  Streptomycin in the therapy of granuloma inguinale. Report of 100 cases (AB) (Mar.) 90
Chesney, L. Parker: Penicillin in treatment of neurosyphilis. IV. Tabes dorsalis (AB) (Apr.) 112
Christensen, C. W.: Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301
Clark, J. W., Jr.: Duration of acquired immunity in experimental syphilis (AB) (Dec.) 359
Cohen, Sidney: Treatment of acute uncomplicated gonococcal urethritis with a single dose water-soluble penicillin preparation (AB) (Aug.) 233
Cohn, Alfred: Ambulatory treatment of early syphilis. An experimental study with report of injection of penicillin in water-in-oil emulsion (AB) (July) 206
Cole, H. N.: Penicillin in the treatment of syphilis in pregnancy (OA) (Apr.) 95
Collins, Harvey Shields: Aureomycin treatment of acute gonorrhea in males (AB) (Nov.) 334
Crowe, Ed:
  Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301
Cross, John B.: Use of crystalline penicillin G in treatment of syphilis in pregnancy (AB) (Sept.) 264
Cumberland, Mary C.: Rate of multiplication of *Treponema pallidum* in normal and immune rabbits (AB) (Nov.) 330
Curtis, Arthur C.:
  Neurosyphilis: Evaluation after two years of treatment with penicillin alone and with a combination of penicillin and malaria (AB) (May) 150
  Studies of the life and motility of *Treponema pallidum* in fertile hens' eggs (AB) (Dec.) 360

Page

Curtis, Arthur C.—Continued
  Treatment of syphilitic primary optic atrophy with penicillin and with penicillin and malaria (AB) (Oct.) 300

D

Davis, Warren T., Jr.: Socioeconomic factors in syphilis prevalence, Savannah, Georgia (OA) (May) 131
Dienst, Robert B.:
  Experimental studies on the pathogenicity of *Donovania granulomatis* (AB) (Oct.) 300
  Oral aureomycin in therapy of streptomycin-resistant granuloma inguinale (AB) (Aug.) 237
  Streptomycin in the therapy of granuloma inguinale. Report of 100 cases (AB) (Mar.) 90
Dowling, Harry F.: The effect of caronamide on the blood concentration of penicillin following oral and intramuscular administration of penicillin (AB) (Sept.) 265
Drew, Ruth: Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301

E

Eagle, Harry:
  Antibody response in rabbits to killed suspensions of pathogenic *T. pallidum* (AB) (Jan.) 24
  Nutritional requirements of treponemata. I. Arginine, acetic acid, sulfur-containing compounds, and serum albumin as essential growth-promoting factors for the Reiter treponeme (AB) (Mar.) 88
  Rate of bactericidal action of penicillin in vitro as a function of its concentration, and its paradoxically reduced activity at high concentrations against certain organisms (AB) (Jan.) 25
  Serologic relationships between five cultured strains of supposed *T. pallidum* (Noguchi, Kroó, Nichols, Reiter and Kazan) and two strains of mouth treponemata (AB) (Mar.) 89
  Therapeutic activity of bacitracin in rabbit syphilis, and its synergistic action with penicillin (AB) (Jan.) 29
Edeiken, Joseph: Observations on penicillin-treated cardiovascular syphilis (AB) (Oct.) 297

NOTE: OA, original article; AB, abstract; NR, Current Notes and Reports.

Page

Eiber, Harold B.: Treatment of acute uncomplicated gonococcal urethritis with a single dose water-soluble penicillin preparation (AB) (Aug.) 233

Eisenberg, Henry:
  Asexual syphilis in children (OA) (Jan.) 7
  Penicillin in abortive treatment of syphilis (OA) (Sept.) 252
  Penicillin in oil and beeswax in treatment of syphilis in clinic patients (AB) (Sept.) 263
  Use of a multiple-copy form as an efficient clerical basis for medical clinics operation (OA) (Oct.) 288

Ercoli, N.: New vehicle for parenteral repository penicillin therapy (AB) (Feb.) 59

F

Falk, Mortimer S.:
  Long-term results in neurosyphilis treated with penicillin alone (AB) (May) 150
  Observations on penicillin-treated cardiovascular syphilis (AB) (Oct.) 297

Farber, Mary Streeter: Necessity for treatment of pregnant syphilitic women during every pregnancy (AB) (Feb.) 53

Farmer, Thomas, W.:
  Acute syphilitic meningitis. Report of 80 cases (AB) (May) 152
  Jarisch-Herxheimer reaction in early syphilis, treated with crystalline penicillin G (AB) (Feb.) 60
  Jarisch-Herxheimer reaction in neurosyphilis treated with penicillin (AB) (July) 207

Finberg, Laurence: Characteristics of the cerebrospinal fluid in lymphogranuloma venereum (OA) (Oct.) 291

Finland, Maxwell: Aureomycin treatment of acute gonorrhea in males (AB) (Nov.) 334

Fleischman, Ralph:
  Antibody response in rabbits to killed suspensions of pathogenic *T. pallidum* (AB) (Jan.) 24
  Therapeutic activity of bacitracin in rabbit syphilis, and its synergistic action with penicillin (AB) (Jan.) 29

Freeble, Charles R., Jr.: Mass public venereal disease education—Ohio fairs (OA) (July) 196

G

Gable, G. Roland: Treatment of gonorrhea with streptomycin (AB) (Oct.) 301

Page

Gammon, George D.: Long-term results in neurosyphilis treated with penicillin alone (AB) (May) 150

Germuth, Frederick G., Jr.: Serologic relationships between five cultured strains of supposed *T. pallidum* (Noguchi, Kroó, Nichols, Reiter and Kazan) and two strains of mouth treponemata (AB) (Mar.) 89

Giacomo, Rosalie: Integration of public health nursing into a marine hospital (OA) (Jan.) 15

Goodwin, Mary Stewart: Necessity for treatment of pregnant syphilitic women during every pregnancy (AB) (Feb.) 53

Gray, A. L.:
  Syphilis contact investigation in a rural county in Mississippi (OA) (June) 165
  Venereal disease case finding in Quitman County, Mississippi (OA) (May) 127

Greaves, Aston B.: Treatment of gonorrhea with streptomycin (AB) (Oct.) 301

Greenblatt, Robert B.:
  Experimental studies on the pathogenicity of *Donovania granulomatis* (AB) (Oct.) 300
  Oral aureomycin in the therapy of streptomycin-resistant granuloma inguinale (AB) (Aug.) 237
  Streptomycin in the therapy of granuloma inguinale. Report of 100 cases (AB) (Mar.) 90

Gross, Benjamin A.:
  Penicillin treatment of syphilitic primary optic atrophy. Interim report (AB) (Nov.) 332
  Syphilitic primary optic atrophy as a cause of blindness; importance of early diagnosis (AB) (May) 152

Grover, Ralph W.: Evaluation of treatment of paretic neurosyphilis (AB) (Feb.) 55

Grund, Robert: Use of a multiple-copy form as an efficient clerical basis for medical clinics operation (OA) (Oct.) 288

Grunstein, Isaak: Ambulatory treatment of early syphilis. An experimental study with report of injection of penicillin in water-in-oil emulsion (AB) (July) 206

Gustafson, Milton H.: Quantitative serologic titer in posttreatment observation of early syphilis treated with penicillin (AB) (Nov.) 335

NOTE: OA, original article; AB, abstract; NR, Current Notes and Reports.

Page

Gyorgy, Paul: Treatment of infantile congenital syphilis. Results with aqueous penicillin alone in sixty infants followed for an average of two years after treatment (AB) (Dec.) 359

H

Hammerman, Steven: Combined treatment of symptomatic paresis with penicillin and fever produced by continuous intravenous typhoid vaccine (AB) (Sept.) 271

Harding, Virginia L.: Effect of temperature variants on quantitative turbidimetric determination of spinal fluid protein, using trichloracetic acid (OA) (Nov.) 325

Harris, Ad:
  Effect of temperature variants on quantitative turbidimetric determinations of spinal fluid protein, using trichloracetic acid (OA) (Nov.) 325
  Penicillin treatment of early syphilis—first four patients after six years (OA) (Dec.) 350
  Quantitative turbidimetric method for determination of spinal fluid protein (OA) (Apr.) 100

Hayman, Charles R.: Rapid treatment of syphilis. A second study of clinic attendance (OA) (Oct.) 285

Heilman, Fordyce R.: Aureomycin: studies on absorption, diffusion and excretion (AB) (Oct.) 304

Henderson, Clair A.: Socioeconomic factors in syphilis prevalence, Savannah, Georgia (OA) (May) 131

Hendricks, Franklin D.: Treatment of gonorrhea with streptomycin (AB) (Oct.) 301

Herrell, Wallace E.:
  Aureomycin: studies on absorption, diffusion and excretion (AB) (Oct.) 304
  Oral use of aureomycin in the treatment of late cutaneous syphilis (AB) (Oct.) 305

Heyman, Albert:
  Morphologic changes in syphilitic lesions during the Jarisch-Herxheimer reaction (AB) (Nov.) 331
  Treatment of ocular syphilis with penicillin (AB) (Sept.) 266
  Use of crystalline penicillin G in treatment of syphilis in pregnancy (AB) (Sept.) 264

Hibbets, Richard S.:
  Syphilis contact investigation in a rural county in Mississippi (OA) (June) 165

Page

Hibbets, Richard S.—Continued
  Venereal disease case finding in Quitman County, Mississippi (OA) (May) 127

Hill, Justina: Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301

Hill, Lyndon M.: Aureomycin: a new antibiotic with virucidal properties. 1. Preliminary report on successful treatment in twenty-five cases of lymphogranuloma venereum (AB) (Feb.) 60

Hirsh, Harold L.:
  Effect of caronamide on the blood concentration of penicillin following oral and intramuscular administration of penicillin (AB) (Sept) 265
  Treatment of gonorrhea with streptomycin (AB) (Oct.) 301

Hoekenga, Mark T.:
  Jarisch-Herxheimer reaction in neurosyphilis treated with penicillin (AB) (July) 207
  Procaine penicillin G in gonorrhea. An experimental evaluation with observations on blood levels and urinary excretion after small doses (AB) (Feb.) 55

Horne, S. F.:
  Neurosyphilis: Evaluation after two years of treatment with penicillin alone and with a combination of penicillin and malaria (AB) (May) 150
  Treatment of syphilitic primary optic atrophy with penicillin and with penicillin and malaria (AB) (Oct.) 300

Hueper, W. C.: New vehicle for parenteral repository penicillin therapy (AB) (Feb.) 59

Hunter, Charles A.: Observation of the Kolmer complement-fixation test and the VDRL spinal fluid test (OA) (Dec.) 347

I

Ingraham, Norman R., Jr.: Treatment of infantile congenital syphilis. Results with aqueous penicillin alone in sixty infants followed for an average of two years after treatment (AB) (Dec.) 359

Iskrant, Albert P.:
  Contact investigation of syphilis (OA) (May) 140
  Syphilis contact investigation in a rural county in Mississippi (OA) (June) 165

NOTE: OA, original article; AB, abstract; NR, Current Notes and Reports.

J — Page

Jenkins, Kenneth H.: Penicillin in the treatment of syphilis in pregnancy (OA) (Apr.) 95

Johnston, Dorothy: Educational program at Alto Medical Center—Alto, Georgia (NR) (Apr.) 120

K

Kahn, Reuben L.: Studies on cardiolipin antigen. V. Standardization of antigen for the Kahn test (AB) (Mar.) 89

Kaiser, Thomas F.: Aureomycin treatment of acute gonorrhea in males (AB) (Nov.) 334

Kanter, Joseph: Vagotomy in treatment of gastric crises of tabes dorsalis (AB) (May) 153

Karpinos, Bernard D.: Efficacy of penicillin treatment of early syphilis in the Army (AB) (Oct.) 299

Katzen, Perry: Treatment of acute uncomplicated gonococcal urethritis with a single dose water-soluble penicillin preparation (AB) (Aug.) 233

Kendell, H. Worley: Fever-chemotherapy in early syphilis (OA) (Mar.) 69

Kierland, Robert R.:
  Oral use of aureomycin in the treatment of late cutaneous syphilis (AB) (Oct.) 305
  Treatment of neurosyphilis with a combination of malaria and penicillin (AB) (Feb.) 56

Kitchen, D. K.: Newer repository penicillin products (AB) (Feb.) 58

Klauder, Joseph V.:
  Penicillin treatment of syphilitic primary optic atrophy. Interim report (AB) (Nov.) 332
  Syphilitic primary optic atrophy as a cause of blindness; importance of early diagnosis (AB) (May) 152

Kopp, Israel: Treatment of late symptomatic neurosyphilis at Boston Psychopathic Hospital. Study of results of penicillin therapy in 394 patients treated between February, 1944 and March, 1948 (AB) (May) 149

Landis, L.: New vehicle for parenteral repository penicillin therapy (AB) (Feb.) 59

L — Page

Lankford, Charles E.: Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301

Laughlin, M. E.:
  Penicillin in abortive treatment of syphilis (OA) (Sept.) 252
  Use of multiple-copy form as an efficient clerical basis for medical clinics operation (OA) (Oct.) 288

Leifer, William:
  Treatment of acute uncomplicated gonococcal urethritis with a single dose water-soluble penicillin preparation (AB) (Aug.) 233
  Efficacy of penicillin treatment of early syphilis in the Army (AB) (Oct.) 299

Lepper, Mark H.: Effect of caronamide on the blood concentration of penicillin following oral and intramuscular administration of penicillin (AB) (Sept.) 265

Lewis, John A., Jr.: Problems of outpatient management of syphilis in the South (OA) (Jan.) 19

Loewe, Leo: Treatment of acute uncomplicated gonococcal urethritis with a single dose water-soluble penicillin preparation (AB) (Aug.) 233

Logan, Myra A.: Aureomycin: a new antibiotic with virucidal properties. 1. Preliminary report on successful treatment in twenty-five cases of lymphogranuloma venereum (AB) (Feb.) 60

London, Irving D.: Fever and penicillin therapy in treatment of congenital syphilitic interstitial keratitis. Preliminary report of nine cases (AB) (Feb.) 57

Longacre, Alfred B.: Results of systemic administration of the antibiotic, bacitracin, in surgical infections, preliminary report (AB) (July) 204

Lord, Richard E.: Characteristics of the cerebrospinal fluid in lymphogranuloma venereum (OA) (Oct.) 291

Lyons, R. H.: Newer repository penicillin products (AB) (Feb.) 58

Mc

McCain, John R.: Use of crystalline penicillin G in treatment of syphilis in pregnancy (AB) (Sept.) 264

McDermott, Elizabeth B.: Studies on cardiolipin antigen. V. Standardization of antigen for the Kahn test (AB) (Mar.) 89

NOTE: OA, original article; AB, abstract; NR, Current Notes and Reports.

Page

- McLeod, Charlotte: Preservation and inoculation studies on *Treponema pallidum* (OA) (Apr.) 104

M

- Magnuson, Harold J.:
  - Current concepts of immunity in syphilis (AB) (May) 148
  - Duration of acquired immunity in experimental syphilis (AB) (Dec.) 360
  - Rate of development and degree of acquired immunity in experimental syphilis (AB) (Feb.) 54
  - Treatment of asymptomatic neurosyphilis in white mouse (AB) (Aug.) 230
  - Treponemal immobilization test of normal and syphilitic serums (OA) (Nov.) 309
- Mahoney, J. F.:
  - Penicillin therapy of early syphilis. IV. (OA) (May) 125
  - Penicillin treatment of early syphilis—first four patients after six years (OA) (Dec.) 350
  - Role of cardiolipin antigens in serology of syphilis (OA) (Aug.) 217
- Mahoney, Vincent P.: Combined treatment of symptomatic paresis with penicillin and fever produced by continuous intravenous typhoid vaccine (AB) (Sept.) 271
- Markson, Leonard S.: Vagotomy in treatment of gastric crises of tabes dorsalis (AB) (May) 153
- Marshak, Lydia: Granuloma inguinale. Review of literature and report of 97 cases, with a note on streptomycin therapy (AB) (July) 205
- Maxwell, Richard W.: Jarisch-Herxheimer phenomenon in late syphilis. Probable fatal reactions to penicillin (AB) (Aug.) 229
- Mayer, Manfred M.: Immobilization of *Treponema pallidum* in vitro by antibody produced in syphilitic infection (AB) (Sept.) 268
- Meleney, Frank L.: Results of systemic administration of the antibiotic bacitracin, in surgical infections, preliminary report (AB) (July) 204
- Merrell, Margaret: Results of Nationwide study of penicillin in early syphilis. Report of Central Statistical Unit. I. Amorphous penicillin in aqueous solution (AB) (July) 202
- Messinezy, D. A.: Prevalence of syphilis in pregnant women in Athens, Greece, from 1935 to 1940 (NR) (May) 155
- Meyer, George P.: Syphilitic primary optic atrophy as a cause of blindness; importance of early diagnosis (AB) (May) 152
- Miller, C. Phillip: Experimental gonococcal infection of the rabbit's eye (AB) (Feb.) 54
- Moore, Joseph Earle: Cardiovascular syphilis. Summary of recent information, with special reference to treatment with penicillin (AB) (July) 204
- Morse, John W.:
  - Attitude of venereal disease patients toward clinics and rapid treatment centers (OA) (Oct.) 275
  - Socioeconomic factors in syphilis prevalence, Savannah, Georgia (OA) (May) 131
- Morton, Harry E.: Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301
- Mulherin, John L.: Extragenital chancres. Survey of 219 cases (AB) (Jan.) 22
- Musselman, A. D.: Rate of bactericidal action of penicillin in vitro as a function of its concentration, and its paradoxically reduced activity at high concentrations against certain organisms (AB) (Jan.) 25

N

- Nelson, N. A.: The baffling case of Baby T. (OA) (Sept.) 257
- Nelson, Robert A., Jr.:
  - Factors affecting the survival of *Treponema pallidum* in vitro (AB) (May) 147
  - Immobilization of *Treponema pallidum* in vitro by antibody produced in syphilitic infection (AB) (Sept.) 268
- Nicholson, F. P.: Penicillin therapy of early syphilis: IV (OA) (May) 125
- Noojin, Ray O.: Fever and penicillin therapy in treatment of congenital syphilitic interstitial keratitis. Preliminary report of nine cases (AB) (Feb.) 57
- Norton, Dorothy H.: Neurosyphilis: Evaluation after two years of treatment with penicillin alone and with a combination of penicillin and malaria (AB) (May) 150

O

- O'Leary, Paul A.:
  - Oral use of aureomycin in the treatment of late cutaneous syphilis (AB) (Oct.) 305

NOTE: OA, original article; AB, abstract; NR, Current Notes and Reports.

Page

O'Leary, Paul A.—Continued
- Treatment of neurosyphilis with a combination of malaria and penicillin (AB) (Feb.) 56

Ozog, J. J.: Efficacy of penicillin treatment of early syphilis in the Army (OA) (Oct.) 299

P

Packer, Henry: Spinal fluid and blood complement fixation reversal in neurosyphilis (AB) (May) 151

Pardo, Osvaldo A.: Acute syphilitic meningitis. Report of 80 cases (AB) (May) 152
- Jarisch-Herxheimer reaction in early congenital syphilis. Study of ninety-three patients treated with penicillin alone (AB) (Nov.) 332

Parkhurst, George E.: Comparative studies on mailed spinal fluid specimens (OA) (Jan.) 11

Peters, Erwin E.: Fever-chemotherapy in early syphilis (OA) (Mar.) 69

Peizer, Lenora R.: Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301

Phillips, Cornelia M.: The baffling case of Baby T. (OA) (Sept.) 257

Plotke, Frederick:
- Asexual syphilis in children (OA) (Jan.) 7
- Fever-chemotherapy in early syphilis (OA) (Mar.) 69
- Penicillin in abortive treatment of syphilis (OA) (Sept.) 252
- Penicillin in oil and beeswax in treatment of syphilis in clinic patients (AB) (Sept.) 263
- Penicillin in the treatment of syphilis in pregnancy (OA) (Apr.) 95
- Penicillin in the treatment of early syphilis: 639 patients treated with 2,400,000 units of sodium penicillin in 7½ days (OA) (Nov.) 321

Price, Eleanor V.: Results of therapy by race, sex, and stage of syphilis (OA) (Jan.) 1

Prigot, Aaron: Aureomycin: a new antibiotic with virucidal properties. 1. Preliminary report on successful treatment in twenty-five cases of lymphogranuloma venereum (AB) (Feb.) 60

Pulaski, Edwin J.: Results of systemic administration of the antibiotic, bacitracin, in surgical infections, preliminary report (AB) (July) 204

Puzak, Michael A.: Treatment of gonorrhea with streptomycin (AB) (Oct.) 301

Q

Page

Queally, F. J.: A new vehicle for parenteral repository penicillin therapy (AB) (Feb.) 59

R

Regan, Francis C.: Aureomycin treatment of acute gonorrhea in males (AB) (Nov.) 334

Rein, C. R.:
- Newer repository penicillin products (AB) (Feb.) 58
- Treatment of yaws in the Haitian peasant (AB) (Sept.) 270

Remein, Quentin R.: Socioeconomic factors in syphilis prevalence, Savannah, Georgia (OA) (May) 131

Reynolds, Frank W.:
- Nationwide results in the treatment of early syphilis with penicillin (AB) (Apr.) 110
- Penicillin in treatment of neurosyphilis. IV. Tabes dorsalis (AB) (Apr.) 112

Rider, Rowland V.: Results of Nationwide study of penicillin in early syphilis. II. Amorphous penicillin versus crystalline penicillin G, and aqueous penicillin versus penicillin-oil-beeswax (AB) (July) 203

Rion, J. Wallace: Factors affecting the results of interviewing for contacts (OA) (Dec.) 341

Robinson, Jay A.: Effect of caronamide on the blood concentration of penicillin following oral and intramuscular administration of penicillin (AB) (Sept.) 265

Robinson, Jean M.: Procaine penicillin with aluminum monostearate. Serum concentrations after oral and intramuscular administration (AB) (Sept.) 269

Rodriquez, Arthur A.: Fever-chemotherapy in early syphilis (OA) (Mar.) 69

Rodriquez, Jack:
- Fever-chemotherapy in early syphilis (OA) (Mar.) 69
- Penicillin in the treatment of early syphilis: 639 patients treated with 2,400,000 units of sodium penicillin in 7½ days (OA) (Nov.) 321

Rohwedder, Carma: Use of a multiple-copy form as an efficient clerical basis for medical clinics operation (OA) (Oct.) 288

Romansky, M. J.: Newer repository penicillin products (AB) (Feb.) 58

Rosahn, Paul D.: Unknowns in the biology of syphilitic infection (AB) (Apr.) 110

NOTE: OA, original article; AB, abstract; NR, Current Notes and Reports.

Page

- Rose, Augustus S.: Treatment of late symptomatic neurosyphilis at Boston Psychopathic Hospital. Study of results of penicillin therapy in 394 patients treated between February 1944 and March 1948 (AB) (May) 149
- Rose, Elizabeth Kirk: Treatment of infantile congenital syphilis. Results with aqueous penicillin alone in sixty infants followed for an average of two years after treatment (AB) (Dec.) 359
- Rosenau, Barbara J.:
  - Duration of acquired immunity in experimental syphilis (AB) (Dec.) 360
  - Rate of development and degree of acquired immunity in experimental syphilis (AB) (Feb.) 54
  - Treatment of asymptomatic neurosyphilis in white mouse (AB) (Aug.) 230
- Rosenberg, Arthur A.:
  - A quantitative turbidimetric method for the determination of spinal fluid protein (OA) (Apr.) 100
  - Serologic activity of dipalmityl lecithin, preliminary report (OA) (July) 194
- Rosenthal, Theodore:
  - Ambulatory treatment of early syphilis. An experimental study with report of injection of penicillin in water-in-oil emulsion (AB) (July) 206
  - Treatment of acute uncomplicated gonococcal urethritis with a single dose water-soluble penicillin preparation (AB) (Aug.) 233
- Rowe, Richard J.: Studies of the life and motility of *Treponema pallidum* in fertile hens' eggs (AB) (Dec.) 360

S

- Sackett, Andrew P.: Report of spinal fluid findings in patients who "relapsed" following penicillin therapy for early syphilis (OA) (Aug.) 219
- Sanders, Murray: Aureomycin: a new antibiotic with virucidal properties. 1. Preliminary report on successful treatment in twenty-five cases of lymphogranuloma venereum (AB) (Feb.) 60
- Schuman, Leonard M.: Stimulating venereal disease morbidity reporting by private physicians. I. Follow-up of positive serologic test reports (OA) (June) 160
- Schwartz, B. S.: A new vehicle for parenteral repository penicillin therapy (AB) (Feb.) 59

Page

- Schwemlein, George X.:
  - Fever-chemotherapy in early syphilis (OA) (Mar.) 69
  - Penicillin in the treatment of early syphilis: 639 patients treated with 2,400,000 units of sodium penicillin in 7½ days (OA) (Nov.) 321
- Scott, Virgil: Jarisch-Herheimer phenomenon in late syphilis. Probable fatal reactions to penicillin (AB) (Aug.) 229
- Shannon, R. D.: Case holding in out-patient therapy of syphilis. A study of case-holding experiences in out-patient management of patients treated with penicillin on an ambulatory basis (OA) (Oct.) 281
- Shaw, Carolyn O.: Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301
- Sheldon, Walter H.: Morphologic changes in syphilitic lesions during the Jarisch-Herxheimer reaction (AB) (Nov.) 331
- Sheps, Cecil G.:
  - Reports of North Carolina syphilis studies:
    - III. Evaluation of case-finding measures in control of gonorrhea (OA) (Aug.) 211
    - II. Evaluation of case-finding measures in multiple episodes of infectious syphilis (OA) (July) 187
    - I. Evaluation of case-finding measures in syphilis control (OA) (Feb.) 35
- Shervington, E. Walter: The baffling case of Baby T. (OA) (Sept.) 257
- Skinner, John S.:
  - Jarisch-Herxheimer phenomenon in late syphilis. Probable fatal reactions to penicillin (AB) (Aug.) 229
- Sklar, Benson H.: Stimulating venereal disease morbidity reporting by private physicians. I. Follow-up of positive serologic test reports (OA) (June) 160
- Smith, George C.: Granuloma inguinale—report of 85 cases treated with streptomycin (AB) (Jan.) 26
- Solomon, Harry C.: Treatment of late symptomatic neurosyphilis at Boston Psychopathic Hospital. Study of results of penicillin therapy in 394 patients treated between February 1944 and March 1948 (AB) (May) 149
- Sorenson, R. M.: Case holding in out-patient therapy of syphilis. A study of case-holding experiences in out-patient management of patients treated with penicillin on an ambulatory basis (OA) (Oct.) 281

NOTE: OA, original article; AB, abstract; NR, Current Notes and Reports.

Page

Spoto, Joseph S.: Contact investigation of syphilis (OA) (May) 140

Steiger, Howard P.:
  Observations on penicillin-treated cardiovascular syphilis (AB) (Oct.) 297

Steinman, Harry G.: Nutritional requirements of treponemata. I. Arginine, acetic acid, sulfur-containing compounds, and serum albumin as essential growth-promoting factors for the Reiter treponeme (AB) (Mar.) 88

Stokes, John H.: Long-term results in neurosyphilis treated with penicillin alone (AB) (May) 150

Stoops, Charles W., Jr.: Vagotomy in the treatment of gastric crises of tabes dorsalis (AB) (May) 153

Sullivan, James M.: Vagotomy in treatment of gastric crises of tabes dorsalis (AB) (May) 153

T

Taggart, S. Ross: Treatment of gonorrhea with streptomycin (AB) (Oct) 301

Thayer, J. D.: Evaluation of twelve media for the isolation of the gonococcus (AB) (Oct.) 301

Thomas, E. W.:
  Newer repository penicillin products (AB) (Feb.) 58
  Penicillin in the treatment of syphilis in pregnancy (OA) (Apr.) 95
  Penicillin treatment of early syphilis (AB) (Apr.) 111

Thompson, Frederick A., Jr.: Treponemal immobilization test of normal and syphilitic serums (OA) (Nov.) 309

Trautman, J. A.: Integration of public health nursing into a marine hospital (OA) (Jan.) 15

Trousdale, Helen: Aureomycin treatment of acute gonorrhea in males (AB) (Nov.) 334

Tucker, Harold A.:
  Extragenital chancres. Survey of 219 cases (AB) (Jan.) 22
  Jarisch-Herxheimer reaction in early congenital syphilis. Study of ninety-three patients treated with penicillin alone (AB) (Nov.) 332
  Penicillin syphilotherapy administered during pregnancy. Study of 149 pregnancies during which penicillin was given for early maternal syphilis (AB) (June) 181
  Penicillin syphilotherapy administered prior to pregnancy. Study

Page

Tucker, Harold A.—Continued
  of 111 pregnancies during which additional antisyphilitic treatment was withheld (AB) (July) 201
  Procaine penicillin G in gonorrhea. An experimental evaluation with observations on blood levels and urinary excretion after small doses (AB) (Feb.) 55

Turner, Thomas B.: Rate of multiplication of *Treponema pallidum* in normal and immune rabbits (AB) (Nov.) 330

U

Underwood, Laurence J.: Treatment of neurosyphilis with a combination of malaria and penicillin (AB) (Feb.) 56

Usilton, Lida J.: Attitude of venereal disease patients toward clinics and rapid treatment centers (OA) (Oct.) 275

V

Victor, Frank M.: Observation of the Kolmer complement-fixation test and the VDRL spinal fluid test (OA) (Dec.) 347

W

Watson, John B.:
  Neurosyphilis. Penicillin and malarial fever therapy versus penicillin and vaccine (typhoid) fever therapy (AB) (Oct.) 302

Wax, Louis: Sugar fermentations of gram-negative diplococci isolated from genitourinary tract of penicillin-treated gonorrhea patients (OA) (May) 145

West, Robert: Oral aureomycin in therapy of streptomycin-resistant granuloma inguinale (AB) (Aug.) 237

Willcox, R. R.: A study of nonspecific urethritis in British soldiery (OA) (Sept.) 243

Wong, Y. T.: Spinal fluid and blood complement fixation reversal in neurosyphilis (AB) (May) 151

Wright, Earl O.: Mass public venereal disease education—Ohio fairs (OA) (July) 196

Wright, John J.:
  Reports of North Carolina syphilis studies:
    III. Evaluation of case-finding measures in control of gonorrhea (OA) (Aug.) 211

NOTE: OA, original article; AB, abstract; NR, Current Notes and Reports.

Page

Wright, John J.—Continued
  II. Evaluation of case-finding measures in multiple episodes of infectious syphilis (OA) (July) 187
  I. Evaluation of case-finding measures in syphilis control (OA) (Feb.) 35
Wright, Louis T.: Aureomycin: a new antibiotic with virucidal properties. 1. Preliminary report on successful treatment in twenty-five cases of lymphogranuloma venereum (AB) (Feb.) 60
Wright, R. D.: Penicillin therapy of early syphilis: IV (OA) (May) 125

Z Page

Zeller, William W.: Effect of caronamide on the blood concentration of penicillin following oral and intramuscular administration of penicillin (AB) (Sept.) 265

Zimmerman, Robert J.: Granuloma inguinale—report of 85 cases treated with streptomycin (AB) (Jan.) 26

Zintel, Harold A.: Results of systemic administration of the antibiotic, bacitracin, in surgical infections, preliminary report (AB) (July) 204

SUBJECT INDEX

A Page

Alto Medical Center, educational program [Johnston] (NR) (Apr.) 120
Aluminum monostearate with procaine penicillin, serum concentrations after oral and intramuscular administration [Robinson] (AB) (Sept.) 269
Antibiotics, bacitracin, systemic administration [Meleney et al.] (AB) (July) 204
Antigen:
  cardiolipin, serology of syphilis [Arnold & Mahoney] (OA) (Aug.) 217
  cardiolipin, standardization for Kahn test [McDermott & Kahn] (AB) (Mar.) 89
Antimony potassium tartrate therapy, granuloma inguinale [Marshak et al.] (AB) (July) 205
Arkansas, Hot Springs Medical Center, mailed spinal fluid specimens, comparative studies [Cannefax et al.] (OA) (Jan.) 11
Army, syphilis, early, efficacy of penicillin treatment [Altshuler] (AB) (Oct.) 299
Aureomycin:
  antibiotic, new, with virucidal properties [Wright et al.] (AB) (Feb.) 60
  studies on absorption, diffusion, and excretion [Herrell & Heilman] (AB) (Oct.) 304

Page

Aureomycin—Continued
  treatment, acute gonorrhea in males [Collins et al.] (AB) (Nov.) 334
  treatment, lymphogranuloma venereum [Wright et al.] (AB) (Feb.) 60
  treatment, oral in late cutaneous syphilis [O'Leary et al.] (AB) (Oct.) 305
  treatment, oral in streptomycin-resistant granuloma inguinale [Greenblatt et al.] (AB) (Aug.) 237

B

Bacitracin:
  synergistic action with penicillin [Eagle & Fleischman] (AB) (Jan.) 29
  systemic administration [Meleny et al.] (AB) (July) 204
  therapeutic activity in rabbit syphilis [Eagle & Fleischman] (AB) (Jan.) 29
Bismuth:
  -mapharsen-fever, treatment, early syphilis [Rodriquez et al.] (OA) (Mar.) 71
  -mapharsen - penicillin - fever treatment, early syphilis [Rodriquez et al.] (OA) (Mar.) 79
Blindness, optic atrophy, syphilitic primary, as cause [Klauder et al.] (AB) (May) 152

Note: AB, abstract; E, editorial; NR, Current Notes and Reports; OA, original article; S, statistics.

Page

Boston Psychopathic Hospital, penicillin treatment, late symptomatic neurosyphilis [Kopp et al.] (AB) (May) 149
Britain, soldiery, nonspecific urethritis [Willcox] (OA) (Sept.) 243

C

Cardiolipin:
  antigen, standardization for Kahn test [McDermott & Kahn] (AB) (Mar.) 89
  antigens in the serology of syphilis [Arnold & Mahoney] (OA) (Aug.) 217
Caronamide, effect on blood concentration of penicillin following oral and intramuscular penicillin administration [Zeller et al.] (AB) (Sept.) 265
Case finding:
  campaign, radio programs in (NR) (Sept.) 260
  contact interviewing, factors affecting results [Rion & Abraham] (OA) (Dec.) 341
  contact investigation indices, Jan. 1944 to Dec. 1948 (S) (Dec.) 362
  contact investigation in Illinois, 1948 (NR) (Oct.) 296
  contact investigation, interviewer's aid, Navy Department (NR) (Jan.) 31
  contact investigation of syphilis (E) (Dec.) 339
  contact investigation, rural county, Mississippi [Gray et al.] (OA) (June) 165
  gonorrhea control, North Carolina [Wright & Sheps] (OA) (Aug.) 211
  New Jersey, examination of migrant farm workers, STS (NR) (Feb.) 65
  project, Maryland (NR) (Feb.) 65
  syphilis, contact investigation [Spoto & Iskrant] (OA) (May) 140
  syphilis control, North Carolina [Wright & Sheps] (OA) (Feb.) 35
  syphilis, infectious, multiple episodes, North Carolina [Wright & Sheps] (OA) (July) 187
  venereal disease, Middletown, Ohio (NR) (July) 199
  venereal disease, Navy (NR) (Sept.) 261
  venereal disease, Quitman County, Miss. [Gray et al.] (OA) (May) 127
Case holding:
  in out-patient therapy of syphilis [Sorenson & Shannon] (OA) (Oct.) 281
  out-patient, Virginia, first report (NR) (Mar.) 91

Page

Central Statistical Unit:
  penicillin, amorphous, in aqueous solution, treatment, early syphilis, Nation-wide study, I. [Merrell] (AB) (July) 202
  penicillin, amorphous vs. crystalline G, aqueous vs. penicillin-oil-beeswax, treatment, early syphilis, Nation-wide study, II. [Merrell] (AB) (July) 203
Cerebrospinal fluid in lymphogranuloma venereum [Finberg et al.] (OA) (Oct.) 291
Chancres, extragenital, survey [Tucker & Mulherin] (AB) (Jan.) 22
Chancroid, cases reported, fiscal 1948 (S) (Jan.) 32
Chicago:
  program to "KO-VD" (NR) (Oct.) 295
  Venereal Disease Control Program, multiple-copy form efficient clerical basis for medical clinics operation [Eisenberg et al.] (OA) (Oct.) 288
Children, syphilis, asexual [Eisenberg et al.] (OA) (Jan.) 7
Chile, University medical school, medical reference material needed (NR) (Aug.) 226
Clinics:
  attendance, second study, rapid treatment of syphilis [Hayman] (OA) (Oct.) 285
  attitude of venereal disease patients toward [Usilton & Morse] (OA) (Oct.) 275
  medical, operation, multiple-copy form efficient clerical basis [Eisenberg et al.] (OA) (Oct.) 288
  syphilitic patients treated with penicillin in oil and beeswax [Eisenberg & Plotke] (AB) (Sept.) 263
Columbia University Communications Materials Center: *See* Education.
Complement-fixation test, reversal in neurosyphilis, spinal fluid and blood [Wong & Parker] (AB) (May) 151
Contact investigation: *See* Case finding.

D

Diplococci, gram-negative, isolated from genitourinary tract of penicillin-treated gonorrhea patients, sugar fermentations [Wax] (OA) (May) 145
District of Columbia stars VD patients in documentary radio spots (NR) (Dec.) 357
Donovania granulomatis, pathogenicity [Dienst et al.] (AB) (Oct.) 300
Drugs: *See* individual drug

NOTE: AB, abstract; E, editorial; NR, Current Notes and Reports; OA, original article; S, statistics.

E Page

- Editorial:
  - congenital syphilis (Sept.) 241
  - contact investigation of syphilis (Dec.) 339
  - is the incidence of syphilis decreasing? (July) 185
  - radio as venereal disease case-finding instrument (June) 159
- Education: *See also* Publications; Venereal disease
  - Chicago's program to "KO-VD" (NR) (Oct.) 295
  - color slides illustrating lesions of syphilis (NR) (Aug.) 224
  - Columbia University Communications Materials Center, public appeal materials (NR) (June) 174
  - fellowships in venereal disease nursing (NR) (Apr.) 121
  - film, syphilis, "Feeling All Right" (NR) (Aug.) 225
  - health, including VD, "Facts on American Sports and Health," teenagers (NR) (Aug.) 224
  - newspaper advertisements (NR) (Aug) 224
  - program, Medical Center, Alto, Ga. [Johnston] (NR) (Apr.) 120
  - public health nursing fellowships (NR) (Apr.) 121
  - radio, documentary, District of Columbia stars VD patients in (NR) (Dec.) 357
  - radio, Paul Whiteman airs VD records (NR) (Dec.) 358
  - radio programs support case-finding campaigns (NR) (Sept.) 260
  - VD radio programs "tops" (NR) (June) 176
  - venereal disease, campaign, Middletown, Ohio (NR) (July) 199
  - venereal disease, mass public, Ohio fairs [Freeble, Jr., et al.] (OA) (July) 196
  - venereal disease, radio as public appeal medium (E) (June) 159

F

- Fever:
  - and penicillin treatment, congenital syphilitic interstitial keratitis [London & Noojin] (AB) (Feb.) 57
  - -mapharsen-bismuth-penicillin treatment, syphilis, early [Rodriquez et al.] (OA) (Mar.) 79
  - produced by continuous intravenous typhoid vaccine, and penicillin, treatment, symptomatic paresis [Mahoney & Hammerman] (AB) (Sept.) 271
- Films: *See* Education

G Page

- Georgia:
  - educational program, Alto Medical Center [Johnston] (NR) (Apr.) 120
  - Savannah, syphilis prevalence, socio-economic factors [Bowdoin et al.] (OA) (May) 131
- Gonococcus:
  - experimental infection of rabbit's eye [Miller] (AB) (Feb.) 54
  - isolation, evaluation of twelve media [Carpenter et al] (AB) (Oct.) 301
- Gonorrhea: *See also* Statistics; Venereal disease
  - acute, in males, aureomycin [Collins et al.] (AB) (Nov.) 334
  - cases reported, fiscal 1948 (S) (Jan.) 32
  - control, case-finding measures, North Carolina [Wright & Sheps] (OA) (Aug.) 211
  - patients, penicillin-treated, gram-negative diplococci isolated from genitourinary tract, sugar fermentations [Wax] (OA) (May) 145
  - ratio to syphilis in U. S. Navy [Babione] (AB) (Nov.) 333
  - treatment, streptomycin [Taggart et al.] (AB) (Oct.) 301
  - uncomplicated, treatment, procaine penicillin G [Tucker & Hoekenga] (AB) (Feb.) 55
- Granuloma inguinale:
  - cases reported, fiscal 1948 (S) (Jan.) 32
  - review of literature; treatment with streptomycin and with antimony potassium tartrate [Marshak et al.] (AB) (July) 205
  - streptomycin-resistant, treatment, oral aureomycin [Greenblatt et al.] (AB) (Aug.) 237
  - treatment, antimony potassium tartrate [Marshak et al.] (AB) (July) 205
  - treatment, streptomycin [Chen et al.] (AB) (Mar.) 90
  - treatment, streptomycin [Zimmermann & Smith] (AB) (Jan.) 26
- Greece:
  - Athens, syphilis, prevalence in pregnant women, 1935–1940 [Messinezy] (NR) (May) 155

I

- Illinois:
  - contact investigation, 1948 (NR) (Oct.) 296
  - laws, premarital and prenatal, revision (NR) (Nov.) 328
- Immunity, acquired, duration in experimental syphilis [Magnuson et al.] (AB) (Dec.) 359

NOTE: AB, abstract; E, editorial; NR, Current Notes and Reports; OA, original article; S, statistics.

J — Page

- Jarisch-Herxheimer reaction:
  - early syphilis, crystalline penicillin G, treatment [Farmer] (AB) (Feb.) 60
  - late syphilis, penicillin treatment [Scott & Maxwell] (AB) (Aug.) 229
  - morphologic changes in syphilitic lesions during [Sheldon & Heyman] (AB) (Nov.) 331
  - neurosyphilis, penicillin treatment [Hoekenga & Farmer] (AB) (July) 207
  - syphilis, early congenital [Pardo & Tucker] (AB) (Nov.) 332

K

- Kahn test, standardization of antigen [McDermott & Kahn] (AB) (Mar.) 89
- Keratitis, interstitial, congenital syphilitic, fever and penicillin treatment, [London & Noojin] (AB) (Feb.) 57
- Kolmer complement-fixation test and VDRL spinal fluid test, observation of [Victor & Hunter] (OA) (Dec.) 347

L

- Laboratory methods:
  - cardiolipin antigens in serology of syphilis [Arnold & Mahoney] (OA) (Aug.) 217
  - factors affecting survival of *Treponema pallidum* in vitro [Nelson, Jr.] (AB) (May) 147
  - isolation of the gonococcus, evaluation of twelve media [Carpenter et al.] (AB) (Oct.) 301
  - lecithin, dipalmityl, serologic activity [Rosenberg] (OA) (July) 194
  - quantitative turbidimetric determination of spinal fluid protein, using trichloracetic acid [Harding & Harris] (OA) (Nov.) 325
  - quantitative turbidimetric, for determination of spinal fluid protein [Bossak et al.] (OA) (Apr.) 100
  - rate of multiplication of *Treponema pallidum* in normal and immune rabbits [Cumberland & Turner] (AB) (Nov.) 330
  - spinal fluid specimens, mailed, comparative studies [Cannefax et al.] (OA) (Jan.) 11
  - stable control serum for standardizing sensitivity of diagnostic tests, syphilis [Cannefax] (OA) (June) 169

Page

- Laboratory methods—Continued
  - sugar fermentations, gram-negative diplococci isolated from genitourinary tract of penicillin-treated gonorrhea patients [Wax] (OA) (May) 145
  - treponemal immobilization test of normal and syphilitic serums [Magnuson & Thompson] (OA) (Nov.) 309
- Laboratory tests: *See* Laboratory methods; Name of test.
- Laws:
  - premarital and prenatal, new, Texas (NR) (Nov.) 328
  - premarital and prenatal, revision, Illinois (NR) (Nov.) 328
- Lecithin, dipalmityl, serologic activity [Rosenberg] (OA) (July) 194
- Lymphogranuloma venereum:
  - cases reported, fiscal 1948 (S) (Jan.) 32
  - cerebrospinal fluid in [Finberg et al.] (OA) (Oct.) 291
  - treatment, aureomycin [Wright et al.] (AB) (Feb.) 60

M

- Malaria: *See also* Therapy
  - -penicillin treatment, neurosyphilis [Curtis et al.) (AB) (May) 150
  - -penicillin treatment, neurosyphilis [Kierland et al.] (AB) (Feb.) 56
- Mapharsen:
  - -bismuth-fever treatment, early syphilis [Rodriquez et al.] (OA) (Mar.) 71
  - -bismuth-pencillin-fever treatment, early syphilis [Rodriquez et al.] (OA) (Mar.) 79
  - treatment, neurosyphilis, asymptomatic, white mouse [Magnuson & Rosenau] (AB) (Aug.) 230
- Marine hospital, integration of public health nursing into [Trautman & Giacomo] (OA) (Jan.) 15
- Maryland, case-finding project (NR) (Feb.) 65
- Meetings:
  - American Social Hygiene Association, (NR) (Dec.) 356
  - New York venereal disease seminars (NR) (Dec.) 356
  - symposium, "Recent Advances in the Study of Venereal Diseases," April 7–8 (NR) (Feb.) (Mar.) 64, 91
- Meningitis, syphilitic, acute [Pardo & Farmer] (AB) (May) 152
- Mental hospitals, first admissions for all psychoses and for psychoses due to syphilis, United States, 1922, 1933–47 (S) (Nov.) 337

NOTE: AB, abstract; E, editorial; NR, Current Notes and Reports; OA, original article; S, statistics.

Page

- Midwest Venereal Disease Control Seminar, digest of proceedings available (NR) (Aug.) 226
- Mississippi:
  - Quitman County, venereal disease case finding [Gray et al.] (OA) (May) 127
  - rural county, contact investigation [Gray et al.] (OA) (June) 165
- Morbidity: *See also* Statistics
  - reports, follow-up of positive STS [Sklar & Schuman] (OA) (June) 160
- Mortality: *See* Statistics

N

- Navy:
  - contact investigation, interviewer's aid (NR) (Jan.) 31
  - contact investigation reports (NR) (Sept.) 261
  - ratio of gonorrhea to syphilis [Babione] (AB) (Nov.) 333
- Neurosyphilis:
  - asymptomatic, white mouse, treatment, penicillin-mapharsen-tryparsamide [Magnuson & Rosenau] (AB) (Aug.) 230
  - late symptomatic, treatment, penicillin, Boston Psychopathic hospital [Kopp et al.] (AB) (May) 149
  - paretic, treatment evaluation [Grover] (AB) (Feb.) 55
  - spinal fluid and blood complement-fixation reversal [Wong & Packer] (AB) (May) 151
  - treatment, malaria and penicillin combined [Kierland et al.] (AB) (Feb.) 56
  - treatment, penicillin alone, long-term results [Stokes et al.] (AB) (May) 150
  - treatment, penicillin alone, penicillin and malaria [Curtis et al.] (AB) (May) 150
  - treatment, penicillin in white mouse [Magnuson & Rosenau] (AB) (Aug.) 230
  - treatment, penicillin, Jarisch-Herxheimer reaction [Hoekenga & Farmer] (AB) (July) 207
  - treatment, penicillin-malarial fever vs. penicillin-vaccine (typhoid) fever [Watson] (AB) (Oct.) 302
- New Jersey, case-finding project, migrant farm workers, STS (NR) (Feb.) 65
- New York City, venereal disease seminars (NR) (Dec.) 356
- North Carolina:
  - gonorrhea control, case-finding measures [Wright & Sheps] (OA) (Aug.) 211

Page

- North Carolina—Continued
  - syphilis control, case-finding measures [Wright & Sheps] (OA) (Feb.) 35
  - syphilis, infectious, case-finding measures in multiple episodes [Wright & Sheps] (OA) (July) 187
- Nursing:
  - public health, integration into a marine hospital [Trautman & Giacomo] (OA) (Jan.) 15
  - venereal disease, public health fellowships (NR) (Apr.) 121

O

- Ohio:
  - fairs, mass public venereal disease education [Freeble, Jr., et al.] (OA) (July) 196
  - Middletown, venereal disease campaign (NR) (July) 199
- Optic atrophy:
  - syphilitic primary, cause of blindness [Klauder et al.] (AB) (May) 152
  - syphilitic primary, penicillin treatment [Klauder & Gross] (AB) (Nov.) 332
  - syphilitic primary, treatment, penicillin and penicillin-malaria [Horne & Curtis] (AB) (Oct.) 300
- Out-patients:
  - case holding, Virginia, first report (NR) (Mar.) 91
  - early syphilis, treated by private physicians, Vermont [Aiken] (OA) (Apr.) 107
  - syphilitic, management, problems in the South [Lewis] (OA) (Jan.) 19

P

- Paresis, symptomatic, combined treatment, penicillin and fever produced by continuous intravenous typhoid vaccine [Mahoney & Hammerman] (AB) (Sept.) 271
- Penicillin:
  - effect of caronamide on blood concentration following oral and intramuscular administration [Zeller et al.] (AB) (Sept.) 265
  - effect of concentration on rate of bactericidal action in vitro against certain organisms [Eagle & Musselman] (AB) (Jan.) 25
  - G *See also* Penicillin treatment
  - G, therapeutic efficacy in experimental syphilis produced by five different strains of *Treponema pallidum* [Boak & Carpenter] (AB) (July) 202
  - products, newer repository [Thomas et al.] (AB) (Feb.) 58

NOTE: AB, abstract; E, editorial; NR, Current Notes and Reports; OA, original article; S, statistics.

Page

Penicillin—Continued
  schedules, comparative efficacy, in secondary syphilis (chart) (S) (June) 183
  synergistic action with bacitracin, rabbit syphilis [Eagle & Fleischman] (AB) (Jan.) 29
  treatment, abortive, syphilis [Plotke et al.] (OA) (Sept.) 252
  treatment, ambulatory, case-holding experiences [Sorenson & Shannon] (OA) (Oct.) 281
  treatment, amorphous in aqueous solution in early syphilis [Merrell] (AB) (July) 202
  treatment, amorphous vs. crystalline G; aqueous vs. penicillin-oil-beeswax in early syphilis, nation-wide results [Rider] (AB) July) 203
  treatment, aqueous alone in infantile congenital syphilis [Rose et al.] (AB) (Dec.) 359
  treatment, asymptomatic neurosyphilis in the white mouse [Magnuson & Rosenau] (AB) (Aug.) 230
  treatment, cardiovascular syphilis [Edeiken et. al.] (AB) (Oct.) 297
  treatment, cardiovascular syphilis [Moore] (AB) (July) 204
  treatment, combined with fever, mapharsen, and bismuth, early syphilis [Rodriquez et al.] (OA) (Mar.) 79
  treatment, combined with fever produced by continuous intravenous typhoid vaccine, symptomatic paresis [Mahoney & Hammerman] (AB) (Sept.) 271
  treatment, combined with malaria in neurosyphilis [Kierland et al.] (AB) (Feb.) 56
  treatment, crystalline G in syphilis in pregnancy [Cross et al.] (AB) (Sept.) 264
  treatment, crystalline G. Jarisch-Herxheimer reaction in early syphilis [Farmer] (AB) (Feb.) 60
  treatment, early syphilis [Arnold et al.] (OA) (May) 125
  treatment, early syphilis [Bundesen et al.] (OA) (Nov.) 321
  treatment, early syphilis [Thomas] (AB) (Apr.) 111
  treatment, early syphilis, first four patients after six years [Mahoney et al.] (OA) (Dec.) 350
  treatment, early syphilis in pregnancy [Tucker] (AB) (June) 181
  treatment, early syphilis, Nation-wide results [Reynolds] (AB) (Apr.) 110

Page

Penicillin—Continued
  treatment, early syphilis, quantitative serologic titer in posttreatment observation [Gustafson & Bowen] (AB) (Nov.) 335
  treatment, efficacy in early syphilis in the Army [Altshuler et al.] (AB) (Oct.) 299
  treatment in oil and beeswax in syphilis in clinic patients [Eisenberg & Plotke] (AB) (Sept.) 263
  treatment, in water-in-oil emulsion, ambulatory in early syphilis [Cohn et al.] (AB) (July) 206
  treatment, Jarisch-Herxheimer reaction in neurosyphilis [Hoekenga & Farmer] (AB) (July) 207
  treatment, late symptomatic neurosyphilis, Boston Psychopathic Hospital [Kopp et al.] (AB) (May) 149
  treatment, late syphilis, Jarisch-Herxheimer phenomenon [Scott & Maxwell] (AB) (Aug.) 229
  treatment, new vehicle for parenteral repository [Ercoli et al.] (AB) (Feb.) 59
  treatment, ocular syphilis [Benton, Jr. & Heyman] (AB) (Sept.) 266
  treatment, penicillin alone and penicillin and malaria in neurosyphilis [Curtis et al.] (AB) (May) 150
  treatment, penicillin and penicillin-malaria in syphilitic primary optic atrophy [Horne & Curtis] (AB) (Oct.) 300
  treatment, penicillin in oil and beeswax, syphilis in clinic patients [Eisenberg & Plotke] (AB) (Sept.) 263
  treatment, penicillin-malarial fever vs. penicillin-vaccine (typhoid) fever in neurosyphilis [Watson] (AB) (Oct.) 302
  treatment, primary syphilitic optic atrophy [Klauder & Gross] (AB) (Nov.) 332
  treatment, procaine G in gonorrhea [Tucker & Hoekenga] (AB) (Feb.) 55
  treatment, procaine with aluminum monostearate, serum concentrations after oral and intramuscular administration [Robinson] (AB) (Sept.) 269
  treatment, single dose of water-soluble in acute uncomplicated gonococcal urethritis [Loewe et al.] (AB) (Aug.) 233
  treatment, spinal fluid findings in early syphilis patients who "relapsed" following penicillin therapy [Sackett & Boggs) (OA) (Aug.) 219

NOTE: AB, abstract; E, editorial; NR, Current Notes and Reports; OA, original article; S, statistics.

Page

Penicillin—Continued
  treatment, syphilis in pregnancy [Cole et al.] (OA) (Apr.) 95
  treatment, syphilis, prior to pregnancy, additional treatment withheld during pregnancy [Tucker] (AB) (July) 201
  treatment, tabes dorsalis [Chesney & Reynolds] (AB) (Apr.) 112
  treatment, water-soluble in acute uncomplicated gonococcal urethritis [Loewe et al.] (AB) (Aug.) 233
  treatment, with fever, congenital syphilitic interstitial keratitis [London & Noojin] (AB) (Feb.) 57
  treatment, with fever, early syphilis [Rodriquez et al.] (OA) (Mar.) 76
  treatment with penicillin alone, long-term results in neurosyphilis [Stokes et al.] (AB) (May) 150
  treatment, yaws in Haitian peasants [Rein] (AB) (Sept.) 270
Pennsylvania University, fellowships in venereal disease nursing (NR) (Apr.) 121
Physicians, private, stimulating venereal disease reporting by [Sklar & Schuman] (OA) (June) 160
Pregnancy:
  penicillin prior to, additional treatment withheld during [Tucker] (AB) (July) 201
  syphilis,, Athens, Greece, 1935–40 [Messinezy] (NR) (May) 155
  syphilis, penicillin treatment [Cole et al.] (OA) (Apr.) 95
  syphilis, treatment, crystalline penicillin G [Cross et al.] (AB) (Sept.) 264
  syphilitic women, necessity for treatment during every pregnancy [Goodwin & Farber) (AB) (Feb.) 53
Psychoses, first admissions to mental hospitals for all psychoses and for psychoses due to syphilis, United States, 1922, 1933–47 (S) (Nov.) 337
Publications: *See also* Education
  "A Psychiatric Approach to the Treatment of Promiscuity," American Social Hygiene Association (NR) (July) 199
  "Casanova—The Tale of a Mouse," Navy comic booklet (NR) (June) 175
  "Diagnosis of Syphilis" (NR) (Dec.) 358
  digest of proceedings of Midwest Venereal Disease Control Seminar (NR) (Aug.) 226
  directory, venereal disease clinics (NR) (Jan.) 30
  "Facts on American Sports and Health," baseball edition (NR) (Aug.) 224

Page

Publications—Continued
  "Facts on American Sports and Health," football edition (NR) (Nov.) 328
  "Manual of Serologic Tests for Syphilis" (NR) (Nov.) 327
  revision of "Digest of Laws and Regulations Relating to the Prevention and Control of Syphilis and Gonorrhea" (Pub. No. A 422) and "Digest of State and Federal Laws Dealing with Prostitution and Other Sex Offenses" (Pub. No. A 422a), American Social Hygiene Association (NR) (Jan.) 31
Promiscuity, treatment, psychiatric approach (NR) (July) 199

R

Radio: *See* Education
Rapid treatment centers, attitude of venereal disease patients toward [Usilton & Morse] (OA) (Oct.) 275
Rhine River boatmen, international venereal disease control planned by WHO (NR) (Oct.) 296

S

Serology: *See also* Laboratory methods; Spinal fluid
  dipalmityl lecithin, report [Rosenberg] (OA) (July) 194
  Kolmer complement-fixation test and VDRL spinal fluid test, observation of [Victor & Hunter] (OA) (Dec.) 347
  quantitative titer in posttreatment observation of early syphilis [Gustafson & Bowen] (AB) (Nov.) 335
  stable control serum for standardizing sensitivity of diagnostic tests in syphilis [Cannefax] (OA) (June) 169
  syphilis, role of cardiolipin antigens [Arnold & Mahoney] (OA) (Aug.) 217
Social Hygiene Day, 1950 (NR) (Nov., Dec.) 327, 356
South, problems in out-patient management of syphilis [Lewis] (OA) (Jan.) 19
Spinal fluid:
  and blood complement-fixation reversals in neurosyphilis [Wong & Packer] (AB) (May) 151
  findings in patients who "relapsed" following penicillin therapy for early syphilis [Sackett & Boggs] (OA) (Aug.) 219

NOTE: AB, abstract; E, editorial; NR, Current Notes and Reports; OA, original article; S, statistics.

Page

- Spinal fluid—Continued
  - protein, effect of temperature variants on quantitative turbidimetric determinations, using trichloracetic acid [Harding & Harris] (OA) (Nov.) 325
  - protein, quantitative turbidimetric method for determination of [Bossak et al.] (OA) (Apr.) 100
  - specimens, mailed, comparative studies [Cannefax et al.] (OA) (Jan.) 11
- Statistics, Venereal Disease Division, tables and charts:
  - congenital syphilis reported to the Public Health Service, fiscal years 1941–49, by quarters (Sept.) 273
  - contact investigation indices, Jan. 1944 to Dec. 1948 (Dec.) 362
  - mental hospitals, first admissions for all psychoses and for psychoses due to syphilis, United States 1922, 1933–47 (Nov.) 337
  - penicillin schedules, comparative efficacy, secondary syphilis (chart) (June) 183
  - syphilis, acquired, reported by States and Territories, fiscal year quarters, 1941 to date (chart) (July) 209
  - syphilis and gonorrhea reported by State and Territorial health departments, first quarter fiscal year 1949 (Mar.) 92
  - syphilis and gonorrhea reported by State and Territorial health departments, second quarter fiscal 1949 (May) 156
  - syphilis and gonorrhea reported by State and Territorial health departments, January–March 1949 (Oct.) 306
  - syphilis mortality per 100,000 population, 1900–1947 (chart) (Apr.) 123
  - venereal disease cases and rates per 100,000 population, civilian, continental United States, fiscal year 1948 (Aug.) 239
  - venereal disease cases reported to U. S. Public Health Service by State and Territorial health departments, fiscal 1948 (Jan.) 32
  - venereal disease, diagnostic observations, compiled by State and Territorial health departments, fiscal year 1948 (Feb.) 66
- Streptomycin:
  - treatment, gonorrhea [Taggart et al.] (AB) (Oct.) 301
  - treatment, granuloma inguinale [Chen et al.] (AB) (Mar.) 90
  - treatment, granuloma inguinale [Marshak et al.] (AB) (July) 205

Pag

- Streptomycin—Continued
  - treatment, granuloma inguinale [Zimmerman & Smith] (AB) (Jan.) 2
- Syphilis: *See also* Case finding; Education; Laboratory methods; Neurosyphilis; Publications; Statistics; Venereal disease.
  - asexual, in children [Eisenberg et al.] (OA) (Jan.) 7
  - biology, unknowns in [Rosahn] (AB) (Apr.) 11
  - cardiovascular, penicillin-treated [Edeiken et al.] (AB) (Oct.) 297
  - cardiovascular, summary of recent information, with special reference to penicillin treatment [Moore] (AB) (July) 204
  - congenital (E) (Sept.) 241
  - congenital, analysis of a baffling case [Shervington et al.] (OA) (Sept.) 257
  - congenital, early, Jarisch-Herxheimer reaction [Pardo & Tucker] (AB) (Nov.) 332
  - congenital, reported to Public Health Service, fiscal years 1941–49, by quarters (S) (Sept.) 273
  - contact investigation (E) (Dec.) 339
  - contact investigation [Spoto & Iskrant] (OA) (May) 140
  - contact investigation, Mississippi, rural county [Gray et al.] (OA) (June) 165
  - control, case-finding measures, North Carolina [Wright & Sheps] (OA) (Feb.) 35
  - early, efficacy of penicillin treatment in Army [Altshuler et al.] (AB) (Oct.) 299
  - early, fever-chemotherapy [Rodriquez et al.] (OA) (Mar.) 69
  - early, in pregnancy, treatment, penicillin [Tucker] (AB) (June) 181
  - early, Jarisch-Herxheimer reaction, treated with crystalline penicillin G [Farmer] (AB) (Feb.) 60
  - early, penicillin-treated, quantitative titer in posttreatment observation [Gustafson & Bowen] (AB) (Nov.) 335
  - early, penicillin treatment—first four patients after six years [Mahoney et al.] (OA) (Dec.) 350
  - early, spinal fluid findings in "relapse" following penicillin therapy [Sackett & Boggs] (OA) (Aug.) 219
  - early, treatment, ambulatory, penicillin in water-in-oil emulsion [Cohn et al.] (AB) (July) 206
  - early, treatment, amorphous penicillin in aqueous solution [Merrell] (AB) (July) 202

NOTE: AB, abstract; E, editorial; NR, Current Notes and Reports; OA, original article; S, statistics.

Page

Syphilis—Continued
- early, treatment, amorphous penicillin vs. crystalline penicillin G. aqueous penicillin vs. penicillin-oil-beeswax [Rider] (AB) (July) 203
- early, treatment, out-patient, by private physicians in Vermont [Aiken] (OA) (Apr.) 107
- early, treatment, penicillin [Arnold et al.] (OA) (May) 125
- early, treatment, penicillin [Thomas] (AB) (Apr.) 111
- early, treatment, penicillin, Nationwide results [Reynolds] (AB) (Apr.) 110
- early, treatment, results by race, sex, and stage [Bauer & Price] (OA) (Jan.) 1
- early, treatment, sodium penicillin [Bundesen et al.] (OA) (Nov.) 321
- experimental, immunity, acquired, rate of development and degree [Magnuson & Rosenau] (AB) (Feb.) 54
- experimental, produced by five different strains of *Treponema pallidum,* therapeutic efficacy of penicillin G [Boak & Carpenter] (AB) (July) 202
- experimental, treatment, penicillin and bacitracin [Eagle & Fleischman] (AB) (Jan.) 29
- incidence, decreasing? (E) (July) 185
- infantile congenital, treatment results with aqueous penicillin alone [Rose et al.] (AB) (Dec.) 359
- infectious, multiple episodes, case-finding measures, North Carolina [Wright & Sheps] (OA) (July) 187
- immunity, current concepts [Magnuson] (AB) (May) 148
- late cutaneous, treatment, aureomycin, oral [O'Leary et al.] (AB) (Oct.) 305
- late latent, prognosis [Blum & Barnett] (AB) (Sept.) 265
- late, treatment, penicillin, Jarisch-Herxheimer phenomenon [Scott & Maxwell] (AB) (Aug.) 229
- meningitis, acute [Pardo & Farmer] (AB) (May) 152
- mortality per 100,000 population, 1900–47 (S) (Apr.) 123
- ocular, treatment, penicillin [Benton, Jr. & Heyman] (AB) (Sept.) 266
- optic atrophy, primary, as cause of blindness [Klauder et al.] (AB) (May) 152
- out-patient management, problems in the South [Lewis] (OA) (Jan.) 19
- pregnancy, prevalence, Athens, Greece, 1935–40 [Messinezy] (NR) (May) 155

Page

Syphilis—Continued
- pregnancy, treatment, crystalline penicillin G [Cross et al.] (AB) (Sept.) 264
- pregnancy, treatment, penicillin [Cole et al.] (OA) (Apr.) 95
- prevalence, socioeconomic factors, Savannah, Ga. [Bowdoin et al.] (OA) (May) 131
- ratio to gonorrhea in U. S. Navy [Babione] (AB) (Nov.) 333
- slides, color, illustration lesions of (NR) (Aug.) 224
- treatment, bacitracin, systemic [Meleney et al.] (AB) (July) 204
- treatment, out-patient, case holding [Sorenson & Shannon] (OA) (Oct.) 281
- treatment, penicillin, abortive [Plotke et al.] (OA) (Sept.) 252
- treatment, necessity for, pregnant syphilitic women during every pregnancy [Goodwin & Farber] (OA) (Feb.) 53
- treatment, penicillin-oil-beeswax, clinic patients [Eisenberg & Plotke] (AB) (Sept.) 263
- treatment, penicillin, prior to pregnancy, additional treatment withheld during pregnancy [Tucker] (AB) (July) 201
- treatment, rapid, clinic attendance [Hayman] (OA) (Oct.) 285

T

Tabes dorsalis:
- gastric crises, treatment, vagotomy [Stoops, Jr., et al.] (AB) (May) 153
- treatment, penicillin [Chesney & Reynolds] (AB) (Apr.) 112

Tests: *See* Name of test; Laboratory methods; Serology.

Texas, laws, premarital and prenatal, new (NR) (Nov.) 328

Therapy: *See also* specific disease or drug
- bacitracin, in rabbit syphilis, synergistic action with penicillin [Eagle & Fleischman] (AB) (Jan.) 29
- fever-chemotherapy, early syphilis [Rodriquez] (OA) (Mar.) 69
- malarial fever-penicillin vs. vaccine (typhoid) fever-penicillin in neurosyphilis [Watson] (AB) (Oct.) 302
- necessity for, in syphilis during every pregnancy [Goodwin & Farber] (AB) (Feb.) 53
- out-patient, syphilis, case holding in [Sorenson & Shannon] (OA) (Oct.) 281
- penicillin-malarial fever vs. penicillin-vaccine (typhoid) fever, neurosyphilis [Watson] (AB) (Oct.) 302

NOTE: AB, abstract; E, editorial; NR, Current Notes and Reports; OA, original article; S, statistics.

Page

Therapy—Continued
  syphilis, results by race, sex, and stage [Bauer & Price] (OA) (Jan.) 1
  vaccine (typhoid) fever-penicillin vs. malarial fever-penicillin, neurosyphilis [Watson] (AB) (Oct.) 302
  vagotomy in gastric crises of tabes dorsalis [Stoops, Jr., et al.] (AB) (May) 153
Treponema pallidum:
  factors affecting survival, in vitro [Nelson, Jr.] (AB) (May) 147
  five different strains, therapeutic efficacy of penicillin G in experimental syphilis produced by [Boak & Carpenter] (AB) (July) 202
  immobilization in vitro, by antibody produced in syphilitic infection [Nelson, Jr. & Mayer] (AB) (Sept.) 268
  life and motility in fertile hens' eggs [Rowe & Curtis] (AB) (Dec.) 360
  pathogenic, killed suspensions, antibody response in rabbits [Eagle & Fleischman] (AB) (Jan.) 24
  preservation and inoculation studies [McLeod & Arnold] (OA) (Apr.) 104
  rate of multiplication, in normal and immune rabbits [Cumberland & Turner] (AB) (Nov.) 330
  supposed, five cultural strains and two strains of mouth treponemata, serologic relationships [Eagle & Germuth, Jr.] (AB) (Mar.) 89
Treponeme, Reiter, growth promotion factors [Eagle & Steinman] (AB) (Mar.) 88
Trichloracetic acid, in quantitative turbidimetric determinations of spinal fluid protein, effect of temperature variants [Harding & Harris] (OA) (Nov.) 325
Tryparsamide, treatment, neurosyphilis, asymptomatic, white mouse [Magnuson & Rosenau] (AB) (Aug.) 230

U

United States: *See also* Statistics
  syphilis experts of WHO meet in (NR) (Oct.) 294
Urethritis:
  gonococcal, acute uncomplicated, treatment, water-soluble penicillin preparation [Loewe et al.] (AB) (Aug.) 233
  nonspecific, in British soldiery [Willcox] (OA) (Sept.) 243

V — Page

VDRL spinal fluid test and Kolmer complement-fixation test, observation of [Victor & Hunter] (OA) (Dec.) 347
Venereal diseases: *See also* specific diseases; Education; Publications; Statistics
  campaign, Middletown, Ohio (NR) (July) 199
  case finding, Navy reports (NR) (Sept.) 261
  case finding, Quitman County, Miss. [Gray et al.] (OA) (May) 127
  case-finding project, Maryland (NR) (Feb.) 65
  clinic directory (NR) (Jan.) 30
  consultation service, Virginia (NR) (Sept.) 261
  contact investigation, interviewer's aid (NR) (Jan.) 31
  control, international, among Rhine River boatman, planned by WHO (NR) (Oct.) 296
  control, morbidity reporting by private physicians [Sklar & Schuman] (OA) (June) 160
  control program approved by WHO committee (NR) (Oct.) 295
  education, newspaper advertisements (NR) (Aug.) 224
  Expert Committee on, World Health Organization, report of second session (NR) (June) 176
  patients, attitude toward clinics and rapid treatment centers [Usilton & Morse] (OA) (Oct.) 275
Vermont, out-patient attendance of early syphilis patients treated by private physicians [Aiken] (OA) (Apr.) 107
Virginia:
  out-patient case holding, first report (NR) (Mar.) 91
  VD consultation service (NR) (Sept.) 261

W

World Health Organization:
  Expert Committee on Venereal Diseases, report of second session (NR) (June) 176
  experts meet in United States (NR) (Oct.) 294
  venereal disease control program approved (NR) (Oct.) 295
  venereal disease control, Rhine River boatmen (NR) (Oct.) 296

Y

Yaws, treatment, penicillin, Haitian peasant [Rein] (AB) (Sept.) 270

NOTE: AB, abstract; E, editorial; NR, Current Notes and Reports; OA, original article; S, statistics.

5108

H